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(54) **FELINE MORBILLIVIRUS AND USES THEREOF**

(71) Applicants: **Kwok-Yung Yuen**, Hong Kong (CN);
Patrick Chiu-Yat Woo, Hong Kong (CN); **Susanna Kar-Pui Lau**, Hong Kong (CN)

(72) Inventors: **Kwok-Yung Yuen**, Hong Kong (CN);
Patrick Chiu-Yat Woo, Hong Kong (CN); **Susanna Kar-Pui Lau**, Hong Kong (CN)

(73) Assignees: **THE GOVERNMENT OF THE HONG KONG SPECIAL ADMINISTRATIVE REGION OF THE PEOPLE'S REPUBLIC OF CHINA**, Hong Kong (CN); **VERSITECH LIMITED**, Hong Kong (CN)

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C12Q 1/68 (2006.01)

(Continued)

(52) **U.S. Cl.**

CPC **C07K 14/115** (2013.01); **A61K 39/12** (2013.01); **C07K 14/005** (2013.01); **C07K 16/1027** (2013.01); **C12N 7/00** (2013.01);

(Continued)

(58) **Field of Classification Search**

None

See application file for complete search history.

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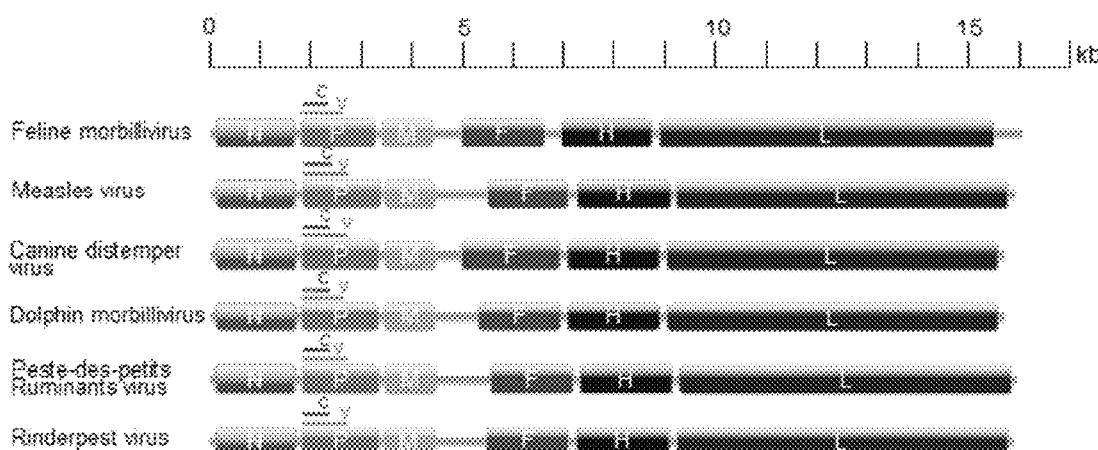
Primary Examiner — Zachariah Lucas

Assistant Examiner — M. Franco Salvoza

(74) *Attorney, Agent, or Firm* — Leason Ellis LLP.

(57) **ABSTRACT**

Described herein are isolated *paramyxovirus*, a *morbillovirus* (FmoPV), nucleic acid molecules, polypeptides and antibodies related to FmoPV and uses thereof. In certain embodiments, the FmoPV is a feline *morbillovirus*. Also described herein is a recombinant FmoPV comprising a modified FmoPV gene or gene segments and uses thereof. Also described is a recombinant FmoPV for the prevention and/or treatment of diseases related to FmoPV or a delivery vector. Also described herein is a diagnostic assay for FmoPV, natural or artificial variants, analogs, or derivatives thereof. Also described herein is a vaccine and a kit containing the vaccine for the prevention and treatment of FmoPV infection. Also provided is a diagnostic kit comprising nucleic acid molecules for the detection of FmoPV.

9 Claims, 45 Drawing Sheets

- (51) **Int. Cl.**
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| <i>A61K 39/12</i> | (2006.01) |
| <i>C07K 14/005</i> | (2006.01) |
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- (52) **U.S. Cl.**
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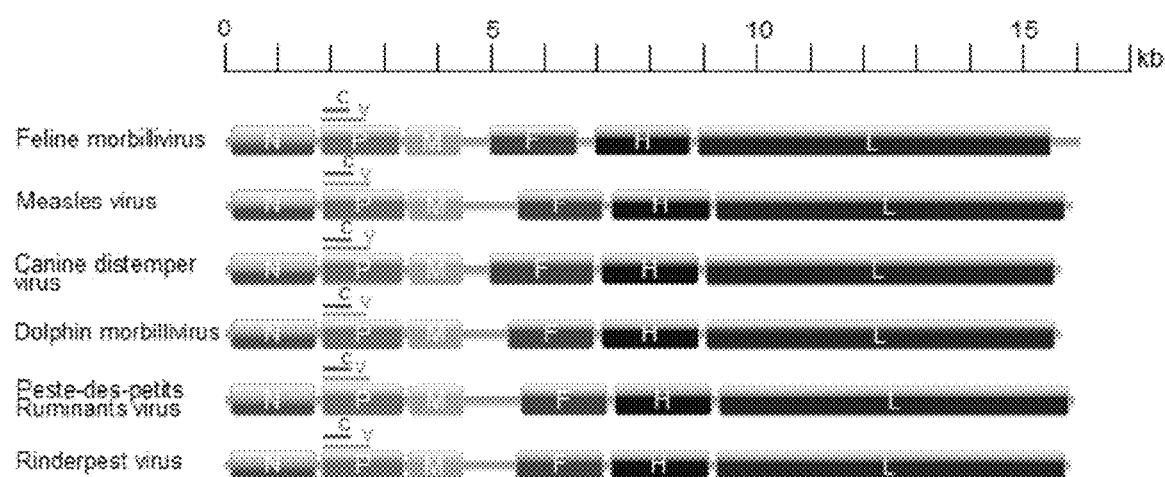
FIGURE 1

Figure 2-1

FmoPV 761U Cats/Hong Kong/2009 16050 bp

ACCAAGACAAAGATGTTGTGACCTATTCTAACGACAAGACTATTATAAATATTTAGGAA
TAACGATTCCATTAGTGAGGTGAGGGGGAGGAATCAGGTATTCCACAATGTCTAGTCTAT
TGAGGTCACTTGCTGCATTAAGAGACATAGGGAGCAACCAACAGCACCGTCAGGTCGG
GTGGTGCAATTAAAGGATTGAAAAATACAATTATTGTTCCAGTTCCAGGGATACTGAA
TTACTACAAGGTCTAATTGTTATTAGATTAGTTATATAATAGGCAATCCGGATACAC
CTTTAAGCACCTCGACGGGAGCAATAATCATTGTTGACCTATTGTCGAATCTCCAG
GTCAATTAAATTCAAAGAATTGCTGATGACCTGATGCAGTTAAATTGGTAGAGGTCA
TTCCTGAAGCTGGTAATCCTGGAGAATTAACCTTGATCTCGAGGGATTAATTAGACA
AGCAAGCTAACAACTTTAAATTGGCTGAGAAAAATGATCAGGGTATTATGTTAGCT
TAGGATTGAGAACCCACCAAATGATGACGATATAACATCTAGCCTGAGATATTCAATT
ATATCCTGGCATCTGTACTTGACACAAGTTGGATTCTCTGGAAAAGCTGTGACTGCTC
CAGATACGGCTGCTGAAGCCGAAATCGTAGATGGATTAAATTATGCAACAAACGTAGGG
TGGATGGTGAAGTGGAGATTGAGCAAGGGATGGCTAGATTGGTAGAAACAAGATTGCGT
CAGATATTACAATAAGCGATTGATGGTAGCATGGTAGATTCTTGACATCAAACGTTCTCCTG
GGACAAGACCCAGGATAGCTGAAATGATTGATATTGATAATTATATTGTAGAGGCAG
GGCTTGCAAGTTCTGTTAACTATTAAATTGGCATAGAGACACGTTATCCAGCACTGG
CACTACATGAGTTCTGGAGAACTAGCCACTATTGAGGGCTTATGAAATTGTACCAAT
CTATGGGGAAATGGCACCACATGGTAATTCTGGAAAATTCAATCCAAACCAGGTTA
GTGCAGGGTCTTATCCTCTGCTATGGAGTTATGCCATGGTGTGGGGTGGAGCTTGAAA
GATCAATGGTGGACTCAATTCACTAGAGAAGCTTCTTGACCTACATATTCAAGACTTG
GTCAAGAGATGGTGGAGGAGATCTTCAGGGATGGTAATAGTCATTGCGAGAGAACTTG
GCCTATCTGATCATGAAACACAACACTGGTCAGCCAGATTGTCAATTGGAGGTGAATCTG
GGATACCTAAATTGATGGATTGAGAGCAATCCAACAACTTTCTAGGAACCAAGATA
ACATAAATGATAGAGGTGAAGATCAGTCATTCAGGGTTACCTGGTCCACTAT
TACCCAGCCGTGACCTAAATCTTCAGGTGATTGATGGAATTAATAGTGGTGTGAAAA

Figure 2-2

ATGTCAGTGACAAACTGAATGAAGGAGTAGGTCCAGACCATGATGTGTCCAGTTCTGCCA
TGGAGAATTGAGAAGATTGGTTGAGTCCACCAACAGAACATAGACACCAAACAGCCAGAAG
CTTCAGGTGTCACCAACCATTATAATGATACTGACCTCTAAAATAATGAGCATAACCC
TAATTGCTTATTATGCAACTCAAATTAAAGAAAAACITAGGACCTCAAGGTTCACAACTGT
TGGCATATCACTAAAATACAGTCAGCTCTCACCCACCACATGTCCTCTCACAAATCCA
GCAAGTCAAACATGGCCTCGAATCTTACAAGAGATCAAAAACAACCCTCCGTCTTCCC
AGATGTCAATCTGCCAGGGAGATTACGAATCCATTAGACAAACAGGAACATCTCAGT
GCAAGGAGGAGCCATTGCGGGAGATAATATTACGTAGGGGTAACAATGACTCAATGTA
TAGCCAAGGACCAAGTCCTCCTATTCAAGTGTAAACAAGAACATCGAAGGACCTACTGG
ATTGATCATTCAAGGACTATGGGATCCAGAGGGTAACCTCTGCATGCTATTGAAAGCGA
TGATGATGAAAACCATTATTCAAGAGATTAATGCCGGCTTCCGCTATCGAAGGACTGGA
TGAACAGGATAATGAGAACTCAATTATTAAACAACCAGGAAATCAGTGTACTGAGGGAGT
GTCTAAGACTGATTCACTCTTAGTTCCCAGGAAACTACACTATCTGTTGGGGATCTGA
TATACCTGGGCAGGAATATCAACCTGTGCCTTTGGATATAACTGTAAATGAAACTCGA
AGATGCAACTGTAAGAAATAGCAACAATATGAAAGGGAACTGCCAATTCTAAATTACT
TGTAAAGCCGCCACCTAGGGTAAAACAAGCGTTGATCACAGTAATCCATTAAAAGGGC
CACAGGAGGGAAATTGCCCTCACCTGGGATGGAGACTACATTATCGAGAGGAGTGGTGC
AACCCCATCTGTACACCCATATACTCAACCTGCAAGCGACTTCAATGTAGGTGCAAGCAA
TGTCCATCAACCTGCCCTAAATGTGAATAATAATTGCAATGATGGTAGGGAACAGCGCC
TAACTCACATAAGATATCGAGGGTGAGTCTGAAATATCTATTCAAGATATATAACTT
GATTCTGGATTTAAGGATGATTACAGGAATTATCAAACAAATTAGATATGGTATTAGA
GATGAAACAAGACATTGACAATCTAAAAAGAACATAGTGCTAAAGTGCAATTGGCTCTATC
AACTATTGAGGGACATCTATCCAGTGTATGATTGCCATCCCTGGTCAGGTATTGATT
CACAGGGATGAGGAAAAGGATCAGATAAATTCTGACTTAAACCAACTGCTAGGAAGGGA
TCATTGTAGAGCATTGAGAAGTTACCAATCCTCTAGATGAGTCTTCAGTCAAGCAAATC
TCCAACAAAACATGTTGCCAAGGTAACAAAAACTGCACTCTCAGAACAGATCAACAAGAA
CGAAACATCTGCAATCAAATTGTTCTAGTGACAGTCATGCAAGCACATCAACCATCAG
ATCAATTATCAGGTCTAATCTCGATCAGGATTGAAAACAAAATTGCTCACAATTCT

Figure 2-3

ATCCCAGATTAGAGGGCAGACAATATTAGAGAATTCTATGAAAAGGTATGATAATTAAAT
AAAGAATAAGAATTAAATATTACAAATCTACATTCAATTAGGTTGTAATTGTCCTCAAT
AAGATTGGTCAGTTCATATATATGGTTATTGATTGTGATAATTATAAAAAACTTAGG
AGCTAAAGTTACTCAGTCATATACAGCATGACTGAGATATTCAACCTTGATGAGAGCTC
ATGGTCAGTCAAAGGGATACTAGATCCGTTAACACCTGATAACCTATCCTGATGGTCAGT
AGTGCCTAAAGTTGAGTTATCGATCCGGTCTAGGAGATCGCAAGAGTGGGGGTATAT
GTACCTACTCTCATGGTGTAGAAGATAGTGAGACTATAATTAGCCGAAAGGAAG
AGCATTGGTGCATTCCATTAGGAGTGGTCAATCAACTGAAAACCCGGAAGACTTGTT
TAAGGAAATATTAACCTCAACATCGTACTCGTAGGACTGCTGGATTAAATGAGAAATT
GGTTTATTATAATACCACACCTCTACATTACTGACCCCCCTGGAAAAAAAGTGTGGCATA
TGGAGGCATTTTAATGCTAATCAGGTCTGCAGTGATACAAGTTCCATACCAATAGACAT
TCCACAAAAATTAGGCCAGTATATTGACTGTTACAAAATTATCTGATGATGGCTATTA
TCAGATCCCAAAGATGATTCAAGATTCAAATCGTCAAATTCTGTTGCATTCAACATCCT
TGTGCATCTGTCAATGGCATAAAATTACTTGACCAATCCAAGGACCCAGATTAAGAAA
TGCTGCAGAAACTGTGATCACATTGATTCAATTGGAAACTTAAACGGAAGAGTAA
TAAGTCTTACTCACCTGAATATTGCAAGAGGAAATAATGAGGCTGGTTAATATTCTC
ATTAGGTGCAATTGGTGGCACAAGCTTGATATTAGATGTACAGGTAAGATGAGCAAACG
ACTACAGGTTATTAGGATTCAAAGGACTTATGTTACCCATTGATGTATGTTAATGA
AGGGCTGAACAAGACCCCTGTGGAGAAGTGAATGCAGAATAGAGAAGGTTCAAGCAGTCTT
ACAGCCATCAGTCCCGAATGAATTAAAGATATGATGATGTTATTATTGATAATACCA
TGGTCTCTCAAGATTAAATAGACTATAACAATAAACAGCTACTAAATAGTATTATG
TATTAAAGTGTACACTGATAATTGCGAATAAAATACACCAGATTAACAGTATAGAGT
TAAGATCTAATTGATATGTGGGTTGGTACTCGATCATTATTAGCTACTGATTATCTA
TATCTTGAATCACCAATGTAAGAGCATCAACAGGTATAAGTTGGATTGCTAGATTG
ACACTTAATTCTCAGAACTAGAATACCCAGATTGTCAAACCTATAACCTGTTAGATTCA
TTAAAGTTAGATTCTGTAAATGTTGATCAATTACTGAGCAATTATAAAAAACTAAG
GACCTAATGTAATAGGAACCCAAACTCCATCCAGTGAGCTCTAAATGCCATGCTTGAAT
ATTAATTATCTAGGGCCTGTCTAACTCAGAACAAAGATCACAAACTAGAGTCTAAAGGAG

Figure 2-4

TGGGTCAAGTCTGAACAATTATCAAGAGCCGAGATTCAAAACTGATTCCCTCTAAACTC
AGAACCCCTAACAAATATCATCCACICAACATCATGAACAGAAATTAGGTTATGATAATT
AGTTCTTATTATTACAGATATTACGATTGCACAAATAGGTTGGATAATTGACTTCG
ATTGGAGTTATAAGTACTAAGCAATACGACTATAAAATAACTACTCTGAACACTGACCAG
TTAATGGTTATAAGATGGTCCTAATATATCATCAATCATTAATTGCACAAACTCGAA
TTAACAAAATATAGAGAGTTAGTCTCAGGGATCATTAGACCAATAATGAGTCATTAGAA
TTAATGAATTACATACATTAACATGAGAGCAGGTTCAGAGAGATTATAGGGCTGTAATA
GCTGGTGAGCCTTAGGAGTGGCAACTGCAGCACAAATAACATCAGGGATTGCCCTACAT
AATTCAATTATGAACAAAAACAAATACAAGAATTGAGGAAGGCTTTAGTACTACCAAC
AAAGCAATTGATGAAATAAGGATTGCAGGTGAAAGAACATTAATAGCAATTCAAGGTGTA
CAGGATTATATTAATAATTATCCCTATGCAGGACAAACTCCAATGTGATATTTA
TCATCACAACTTTCTGTTGCTTACTCAGATATTACAAATATACTAACAGTTTGGG
CCAAGTATACGGATCCTATTACTAGTACAATTCAAGCAGTCAGTCAAGCATT
AATGGTAATCTTCAGGCATTGCTGATGGACTGGGTATACTGGGAGAGACTACGTGAT
CTTCTAGAGAGTAAATCTACTGGCCAGATAATTGAGATGCAGGAGTAACAATATAGG
CTCAATTCAATTACATATCATATTGGCCTGAAGAGTGGTATACCATTATGCCTGATTT
ATTGCTGTTAGGGTTTTAATATCTAATTGATGAGAGAAAGTGGTACGTAAC
TCAAGTATATTGTGCCAACAAAATTCAATTACCAATGTCAACAGAGATGCAAAGATGT
ATTAAGGGCGAGATAAGATTCTGTCCAAGATCCAAGGCAATTGGACATTAGTTAACCG
TTTATATTGACCAAGGTAATTAAATGGCTAATTGTTAGGGATTATGAGATGTTAT
ACTTCAGGACAAGTTAACACAAGACCCAAGTAAATTGATTACGATAATATCGCAAGAG
GAGTGCAAGGAAGTTGGTGTGATGGTATTCTGTTAGGACCTAGAAAATTACCA
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GTCGGGACTGATTTAGCGATTGCTTCAGCTAAACTTAATAATTCTAAGGCATTGTTAGAG
CAATCAGATAAGATTAGATTCAATGTCTAAATTGGATTCTATGAATTCAAGAATAATA
GGATTAATCTTAGCAATTATGATAATCTTATAATCATTATTACTATTATCTGGATCATA
TATAAAAAATGTAGGAATAAGATAATAATTCAAGTACTTCAATTGAACCGCTCACATA

Figure 2-5

CCCCCTTCTTATAACTCACCTCATAGTGTGGTTAAGTCTATTGAGCACTGACCATATGA
TCCACTGTAAATAAGTCCAATGAAAGTATCAATTAAATAATTTGGTAGTGCAATGAGTATT
GATTGTATAATATACTCCTTAAACTAGATAGTGATAAAGGGTTATAGATGATTTCAGTT
ATTTAAATATAATCATATATTGATTTATTACATGACTATTATGTAATTGAATTA
TGTGTCAATTAAATAGCTAATAATATCGTTAATGTACTTATATTGATGGATAGATG
TGTTATATTGTAATCAAGGATTAGTATTTAGAAAAGGAAAGAGTTAATTGTTAA
TTAGTTATTGTGATTCAATTAGAAAAACTTAGGAATCCATGTTAATAAAAATTATTA
TCATGGAGTCCAACAATATTAAGTATTACAAAGATTCTAGCCGTACTTGGTAAAATAT
TAGATGAACACAAAACAATTAAATAGTCAATTGTACAGTTGAGTATCAAGGTAATTACCA
TTATTGCTATTGTAAGCCTGATTGCAACAATAACTATTATCAATGCCACTAGTG
GGAGAACTACCCCTAAATAGTAATACAGACATACTACTCAGCCAACGAGATGAGATTCAA
ACATCCAAGAAAATGATATTGATCGTATTTCCTTGTGATAAAATGCTATGAGTACAGAGC
TAGGACTTCATATTCCCTACCTTATTGGATGAACTTACTAAAGCGATTGACCAGAAAATTA
AAATAATGCATCCTCCTGTGGACACTGTGACTTCTGACCTTAATTGGTGCATCAAACCCC
CTAATGGAATTATCATAGACCCAAAAAGTTATTGTGAGAGTATGGAATTGTCTAAAACCTT
ATGAACTGTTACTTGACCAGTTAGATGTCTCAAGAAAGAAATCACTTATTATAAATAGAA
AGAATATCAACCAGTGCCAATTAGTTGATAATTCAAAGATCATTGCTACTGTCAACA
TACAATCTACACCGAGGTTTAAACTTGGTCACACGGTCAGCAATCAACGTATAACAT
TTGGTCAAGGAACATATAGTAGTACTTATGTTATAACTATCCAAGAAGATGGAGTAACGT
ATGTTCAATATCGAGTGTGAGATCGGATATATTCTGATCAGTTGGTGTATTCCCT
CCTTAATAGTATCGAGAGTGTGCGGATACGTATGCTATTAGGAATGGAATCCTGTACCT
TGACAAGTGATAGACTAGGCAGGTTATTGTATGAAATACACTGACACGATCTATAT
ATGATTATGTTAGCATAAGGGATTGAAATCACTTATATAACAATCCCTCATTATGGTA
AAGTTAATTATACCTACTTAAATTGGTAAGATCAGGAGCCCACATGAGATTGATAAAA
TTTGGTTAACATCTGATAGAGGCCAAATTATCTCTGGTTATTGCAAGCATTGTTACCA
TTACAATTGGAACATATAATAATTATCCCTACAAATGCTTAAATAACCCATGTTTGACA
ACTCTGAGAATTACTGTAGAGGATGGTATAAAAACATAACAGGAACTGATGATGTTCCGA
TATTAGCATACTTATTGGTTGAAATGTATGATGAGGAGGGACCTTAATTACACTTGTGG

Figure 2-6

CAATACCACCTACAATTATAACAGCTCCATCTCATAATTCTCTTACTATGATGACAAAA
TTAATAAAATTAATAATGACTACATCTCACATAGGTTATATTCAAATCAACGAGGIGCATG
AGGTAATTGGCGATAATTGAAGGCTATCCTCTAAACAGATTGTCTGATGAACATC
CTAACCTGACTGCCTGTAGACTCAATCAGGGTATTAAGGAGCAATACAAGTCTGACGGAA
CAATAATTCAAATTCTGACTTATTGATATAACAAGAACGAATGTACATTACAGTTAAAG
CTATTCCACCAGCAGGTAACTATAACTTACAGTTGAGTTGCATTCTAGATCAAACACAT
CCTATGTATCGTTACCAAAACAGTTAATGCTAAGTATGACAAATTACATCTGAGTGCT
TTAGCTGGACAAATCCTGGTGGTGTGCTCTGATAACCCAGTTTCATTAGTTGGAATG
AATCCCTTCTGTTGATACTGCCATTTCAATTAAAGCTGAAATGAACACATCAAT
CTATAGTTGATAGTTGTCAAAACATTAGCTAATTGGGTTAAGAAATAGGAAATGAAA
TTACCAATATCTAATTAGATGTATGTTCAAGCTAAATTACAAAAAAACTTAGGAGTCAGAG
ACTTCGTTGCAATGGAGCAGTCAGACTACCAAGATATTCTATACCCGGAAGTACATCTTA
ACAGTCCTATAGTAATTCCAATTAGTAGGTATTTAGAATACGCCAAATTGCTCATA
ATCAACAATTATCAGACCGTACAATTATCAAGAATATTCAATTAGATTAAGGAACGGAT
TTAATAGTTCAAGGGTACAGGTACTATCAGCTATGGGTGAAATTATCAACAAAATTAGAA
ATAAAATATCTAATTATTCACACATACCTTACCTGAATGCAACCAAAACTATTGCAA
TAGTAGATCCAGAACTAACATCAAAATTAGAATCTCTCTAAACAAAGGTGACACACTGT
ATCTCAAGATTGATCGATCAGATATCATAAAATGTTTGTAGATTGAAAATGAAAATGAATA
TAAAGAATGATCTCTTAATGACAATAGTCATTGATTCTAGATCTTCTTAATTATCA
AAGGATCTCAGTGGTCTTCCCTTTTATTCTGGTTCTATCAAACACTGAAACTAGAA
GCTGTATTGCCAAATCAAAGACTCGTGTAGATCACAATATCGGCCTCACTTATCAG
AGACTAAGAGAATTACATTGGTTGTTACATCTGATCTGATTACAATTGATCATATTA
ATAAAATGTATATTCTGACTTTGAGATGCTGTTAATGTATTGCGATGTGATAGAAG
GTCGGTTAATGACTGAAACAGCTATGAGCTTGGACTGTCGGTTACCAATCTATTGCCAA
GAGTGCAATATATGTGGATTACTAGATGGAATGTTGAAAGTTAGGCAATCAATTAT
ATTCAAGATTGGGAACATTCTGCATCACTGCTTCCGAGTTAGAAGAAATTATAT
TTGACAAAACCCCTTGATCCTTGTATGAAAATTAAATTAGGGCTTGATTACA

Figure 2-7

TTTATTTGACAGGTGATATTCACTAAGTCAGAAGTTTTCTTTTTAGAAGTTTG
GTCATCCTTTTTAGAGGCACAAAATGCTGCTAATAATGTAAGGAAGTATATGAATAAGC
CTAAGGTAATATCATATCAGACTTAATGCAAGGACATGCGATTTTGCCTATTATAA
TAAATGGATTAGAGACCGCCACGGGGAACATGCCCTCTGGAGTTACCAAATCATG
CATCTGCTGTAATTAGAAATGCCAGTTATCTGGAGAAGGGTAACATCTGAACAATGTG
CTCAACACTGGAGATCCTTTGTGGATTAGATTAAATGTTTATGCCATTGAGTCTAG
ATAGTGACCTTACAATGTACCTTAGAGACAAAGCGCTGTCACCTGTCAGAAATGAGTGGG
ATTCACTTATGCTAAGGAGTATTAGGTATAATCCAGGATTACCCACAAGTCCAGAA
GATTGGTAAATGTATTCTAGAAGATGATAAGTTGACCCATATGAAATGATCATGTACG
TGATAAAATGGTGATTACTTAAGAGACAAAGAGTTAACCTTCATACAGCCTAAAGAGA
AAGAAATTAAAGAGGTAGGTGATTGTTGCTAAATGACCTATAAGATGAGGGCTTGTC
AAGTAATAGCTGAAACCTGATTGCCAATGGAGTAGGGAGTTTCAAAGATAATGGAA
TGGCAAAAGATGAACATAAACTAAACTAAGACGTTACACAAATTAGCCATTCAAGGTGTAC
CTAAAGATAATTCTAAACCTTATTTAGATGAATGTTGGAGCAAGTAATTGACAATGTT
CAAGTAGTACACAGATAAGGGAACAGACTATGAATTCAACATCAAATAGGGAAATTGAAT
CAAAGTCTCTAGGGCACGTCTTAATAATAGAGATATCTAAAGGGCAAGAGAGATTGCA
ACAAACAAGTAAAGTATCCTCAAACACCGAGTATTGAGACTATCAGTAGTTCAAA
CTACTGACCTTAAAAGTATTGCTTAACGGCGATATGAATCAAGTAGTATGTTGAG
AGAGACTTAATGAAATTATGGACTGCCTGGATTTCCAGTGGCTTCACAAGATTGG
AGAAATCTGTTCTACGTTAGTGATCCATCTAGTCCACCTGACTTTGATCAACATGTCG
ATATAGAATCAGTCCAAATGACCATACTTATCAAGTACCCGATGGGTGGAATAGAGG
GGTTCTGTCAAAATTATGGACCATTAGTACAATTCCGTTCTATATTAGCAGTTTG
ATACAGGGGTTAGAATCTCATCATTGGTCAAGGCATAACCAGGCAATTGCAAGTAACCA
AAAGAGTTCCGTCACTTGGAGTTACTCAAAGAAAAAGGAAGAATCAACTAAATAACAA
CACAATATTCTTAATTAGACAACGCTTACACGATATAGGTATGAATTGAAAGCAA
ATGAGACTATTATCCTCTCATTCTTTACTCTAAAGGTATTATTGATGGAA
TACTTCTCTCCCAGGCACTTAAAGTATTGCAAGATGTGCTTTGGTCTGAAACGATTG
TTGATGAGACTAGGTCACTGCAGTAATATCTACGACACTCGCAAAGGCAATTGAAA

Figure 2-8

GGGGTTATGATAAATTGTGGCGTACGCTATCAATATTATAAAAACAATACATCAGGTGT
TGATTCATTCCTTACGATTAATCCTACTATGACACCAGACATTACAGAACCTTCT
ACAAGAGTTAGATCTACTTAAGAACATCTAGTTCTGATTCCCTGCACCATTAGGGGCATGA
ACTATATGAACATGAGCAGGTATTTGTTAGGAATATAGGAGATCCCATTACTGCTTCAT
TTGCTGATATAAGCGCATGATTGAATGTGGGTGTTAGGATGAGTATTCTGTACAA
TAATGTACCAAAATGTGGTCCCTCAAATACCTAGACTGGCTAGTGATCCTTATTCAA
TAAACCTTCCTTATAGCCAAAGTATGACCAAGGTTAAAAAATGTAACGGCAAGATATG
TACTTATGCATAGTCCCAACCCATGCTCAAAGATTGTTCCATGAAAAGTCTCAGGAAG
AAGATGAAATCCTTGCTGAGTTCTGTTAGACCGACACTTAATAATCCCTAGAGCAGCAC
ACGAGATTTATCAAATTCACTAACAGGTGCTAGAGAACATCTATAGCAGGTATGCTTGACA
CTACTAAGGGTTAACCGTGCTAGTATGTCAAGAGGTGGGTTGACCTCATCACTTGT
TAAAATTATCAACATATGATTACCAACAGTTAGAACATGTCTTGAATGGCTTATGCTC
CTACTACGGGAATTGCTGTAAGCGTTGATTCTGCTCTGTATTCTTAGCTAACGACCATCC
GGAAGAGAACATGTGGGTCACCTAACTAAAGGAAGGGAGATTATGGGTTAGAAGTACCTG
ACATTGGAAATGTATGCAAAACAATATTATTGTTGATCACGAAGAGATTGTTACTCATGTA
TTCAAGGATCAAGATATTACATGGTTTTGTACCTTCAAATTGTCAACTCGATCAA
TAAATAAGTCAACAAATTCTCTCCGAGTACCTTATGTTGGATCAACAACTGAAGAAAGGA
GTGATATGAAGTTGTCATATGTGAGGTACCTAGTCGCCACTAAAGCAGCAGTCGAA
TTGCAGCAGTATACATGGCTTATGGTGTGATGATAATTGTCTTGGCATGAAGCTTGG
ATTAGCAAGGACTAGAGCAAATATTACTTTGACGAACCTAAATAACACCTATAG
CTACATCTACAAATTAGCACATAGATTGAGAGATAGAACACTCAAGTTAAATATTCA
GAACCTTCTTAGTAAGAGTGGCACGCTATACAACAAATCTAATGATAATATGCTTCA
TTATTAAACAAAAAGTCGATACTAATTGTCTACCAGCAAGGAATGTTATTAGGTT
TGAGTATATTAGAACATATTCAAGATACTGTACAAGTACTGGACAGTCACACTGTAA
TTCACCTACATGCAGATGTTAATTGTTGTATAGTACAGATGACTGATCAGCCTTATACAC
CAAGCTTAAACAAAAAGCTACCTGATATTAGGCCATTAAATAAAACTGATATATGATC
CGGCTCCTATAATCGATACCGATGCGCTAGGCTATATTCCCAAAATACCTGTCACATT
TAATAGATTCCCAAGTTGGTCAACTACTCAGCTAACACAGTGTGGCGAAAGTGGTGG

Figure 2-9

CGGTATCCATTGAGAATTAAATTACAAAAGCTAGTAAAGACCATCTCAATGAGATAATAG
CAGTTGTTGGTGATGATGATATCAATAGCTTATTACAGAATTCTACTTGTGATCCAC
GTCTGTTACAÇTATATTAGGCCAATACACATCATTACAATGGCATATGAAGTCATT
ATCATAGACCAGTGGTAAATACCAGATGGCTGAAGTGTGCATAATTGCTGTCAAGAG
CTAGTAGAGGTATATTCAACATATTGACCAATGCCTTAGCCACCCCAGAGTCTACAAAA
GATTCTGGAGTGTGGTTATTGGAGCCTATTATGGCCCTATATAGGAAGTCAAAATC
TACATAATGCAATGATTGATTATATCTATAATGCATACATTACTTATTGGATGCTTATT
TATCTGATCAAGTAGATGATACTGATATTATAATATGTGAAACAGAGGAGACATGTTGG
CGAACATCGAATTGACAATTATCAAAGCAGACACTTAGCTGTGCTTATAGATCTGTATTGTG
ATTCCACTAGATGTCCAATATAAAAGGGCAGATAACAATTATGAGAAACTCAATTCTTA
GATCTTCATTGATAATGAGAGGAGAACAAATCCACTCGGTTGACATGGAACCTTGACC
CGTTACTCGTGGATCATTAGCTGTCTATTACGTATCTGAGGAGAGGTATTATAAAC
AGATGAGGTTAAGATTGATCCAAGTGTATCGTTGAACTATCTAGGATGATTAAGCCTG
ATGCGGTTATCAAGCACCTAAAATTCCGTCATGGGCTCTATAGATATCAACCCCTG
AAGTAAATGACCTTAATGTAATTGGAGAGCTGAATAGCAAATGAAAGACATTCTA
TTGGACAGATTAGGATACAGAATTATGAAATACATGCATATAGGAGGATCGGAGTTAATT
CAACTGCATGTTATAAAGCTAGAGCTATTGCTGTCTAAATCGGTTATGTCTAAC
CATCAGGTGCATTGTTTAGGTGAAGGAGCAGGATCAATGCTGGTCACATACCGTGCTT
TTGTCCTTAAGACAATTATTATAATAGTGGTATTCAAGTCAAATGTTAGGGCC
AGAGAGAATTGAGTCTATATCCATCTGAAGTGGCACTAGTTGACAACAAAAATCGCTGG
CTAATGACCCCAATATCAAAGTCTTGTCAATGGTAAACCAGAGTCTACGTGGTTGGAA
ACATCGACTTTGCTTATATTCTTAGCCACATTGAGACCTCAAGCTTGACATTGATAC
ATAGTGATATTGAGTCCAGCTTAAGCAAGACGAAGAATAAAATTCTTGAGGAGCTGTGCC
ACATTCTGTCAATGGCACTCATTGGGGAAAATCGGATCTTATTAGTTGTCAAGTTAT
TACCAAGGGTCGGTGAECTACGTATTGCAGGTATGCATCGGAATTCTATCAAC
AAAGCCTCCTGTTACCTAGGTTAGTAACATGTCATCATCTGAGGTTACTATATAG
GGATTCACCTCAATACAAATCGATTGATTGATCCTGATAGAATAGTACAATACATAGTTA
GAAATTACAACCAACTCCAGTTACATTGTCTATATTGAAACTAAGTATAGAA

Figure 2-10

ATAATATGGTACAAATTATGGACTGTGCTTGTCAAGACGGACACAAAAGTGATTACCTGT
CATCAATTACAAAAAATAGAGAACGTTCTCTGTCACTGTGGGTAGAATGAAATGGACCTA
AGATTATACAGCAATTATCAGGACATGACTATGCTAATGGGAGACTAGTCTAGAATCAA
GTATAATGATATTAGTAGAGAATATCTTAATGCAACTATACAAGGCCGGAAACATTAG
GCTGTTTCACCTTACCCAGTCTTACATGAGAGTCAGTTAAGAGAAATTAATAAGTGA
TTGCATTGAAATATGTTGTATATCTACTCTTTATTCAAGCTCTACATTATCTAGTAAAC
AAATAATGAGTAATCTAGAAAGGAATATTGATGTATGATTGAGAGATGAATTTC
TATCAAGATTGTCAGCAAATTACAAGAAAAAGGTGATGTCACAAGAAGTCAAAACACCT
GGATCTTAATCTGATACTCCGACACGAAAAGCATTATATAAGITAGTAGGTTATTCA
TAATAATTAAATCATGTATGATGAGGTATGATTATCCATCTTAAAGAGTAAGATAA
TATCAGATGTATGATAACCAATTAAAGTATTACTTTGAATTGAAAGGTTGCTCAATTACA
CGCTTTTAGTAATCGGGTTTATTCCAATTAGGGCAATTAGAAAAACTCAACGGT
TAGTCGAGCCGAATTCCATTCCATATAAGTTATTTATAATCTGGATAAGACTTTGT
TTAGAATTATAACAGTAATACTAATTATGAATGGAAGACAATTGATATCTAGTGTGAAT
TTTATGTTATGTGTCTAACCTTACTCACTATAATTGTTCTTATTGAGAATTAA
ATTATAGGTGTTATGTGTTATGTGATGGGAACCACAGTGCTGACATTATAACCA
TAGGTATTGTATGGGATAGTGTATTACTACCAATGTACAATCTCATATGTCGGACCC
CTCAACCTCCTCCTTATAGTTGAGTTCTGGAAAAACACAAAAGATGATCTTGAGTAAT
TGTACGGACCTATAGCTTCTTGTCTGGT

Figure 3-1

FmoPV 776U Cats/Hong Kong/2009 16050 bp

ACCAAGACAAAGATGTCTGTGACCTATTCTAACGACAAGATTATTACTAAATATTTAGGAA
TAACGATTCCATTAGTGAGGTGAGGGAGGAATCAGGTATTCCACAATGTCTAGTCTAT
TGAGGTCACTTGCTGCATTAAAGAGACATAGGGAGCAACCAACAGCACCGTCAGGTTCA
GTGGTACAATTAAAGGATTGAAAAAATACAATTATTGTTCCGGTCCAGGGGATACTGAA
TTACTACAAGGTCTAATTGTTATTAGATTAGTTATATAATAGGCAATCCGGATACAC
CTTTAACGCACCTCGACCGGAGCAATAATATCATTGTTGACCCATTGTCGAATCTCCAG
GTCAATTAAATTCAAAGAATTGCTGATGACCTGATGCAGTTAAATTGGTAGAGGTCA
TTCCTGAAGCTGGTAATCCTGGAGAATTAACCTTGATCTCGAGGGATTAATTAGACA
AGCAAGCTCAACAATACTTAAATTGGCTGAGAAAATGATCAGGGTATTATGTTAGCT
TAGGATTGAGAACCCCTCAAATGATGACGATATAACATCTAGTCCTGAGATATTCAATT
ATATCCTGGCATCTGTACTTGACACAAGTTGGATTCTCTGGCAAAAGCTGTGACTGCTC
CAGATACGGCTGCTGAAGCCGAAAATCGTAGATGGATTAAATTATGCAACAAACGTAGGG
TGGATGGTGAAGTGGAGATTGAGCAAAGGATGGCTAGATTAGTGAGAAACAAGATTGCGT
CAGATATTACAATAAGGCATTGATGGTAGCATTAGTTCTGACATCAAACGTTCTCCTG
GGACAAGACCCAGGATAGCTGAAATGATTGTGATATTGATAATTATATTGAGAACAG
GGCTTGCAAGTTCTTATTAACCATTAAATTGGCATAGAAACACGTTATCCAGCACTGG
CACTACATGAGTTCTGGAGAACTAGCCACTATTGAGGGCTTATGAAATTGTACCAAT
CTATGGGGAAATGGCACCATACTGGTAATTCTGGAAAATCTCAATCCAAACCAGGTTA
GTGCAGGGTCTTATCCTCTGCTATGGAGTTATGCAATGGGTGCGGGTGGAGCTGAAA
GATCAATGGGTGGACTCAATTCACTAGAGCTTCACTAGAAGCTTCTTGACCCGACATATT
GTCAAGAGATGGTGAGGGAGATCTCAGGGATGGTTAATAGTCATTGCGAGAGAAACTTG
GCCTATCTGAGCATGAAACACAACTGGTCAGCCAGATTGTCATTGGAGGTGAATCCG
GGATACCTAAATTGATGGATTCAAGAGCAAATCCAACAACTTTCTAGGAACCAAGGATA
ACATAGATGATAGAGGTGAAGATCAGTCAAATTGATATCAGGGTTACCTGGTCCACTAT
TACCCAGCCGTGACCTAGATCTTCCGGTATTGATATGGAATTAAATAGTGGTGTGAAAA
ATGTCAGTGACAAACTGAATGAAGGAGTAGGTCCAGGACCATGATGTGTCAGTTCTGCCA

Figure 3-2

TGGAAGAATTGAGAAGATTGGTTGAGTCTACCAACAGAACATTGACACCAAACAGCCGGAAG
CTTCAGGTGTCACCAACCATTATAATGATACTGACCTCTAAAATAATGAGCATA
TAATTGATTATGATAACTCAAATTAAAGAAAAACTTAGGACCTCAAGGTTACA
TGGCATATCACCAAAACACAGTCAGCTTCACCCACCCATGTCTCACCA
ACAAGTCAAACATGCCCTCGAACTTTACAAGAGATCAAAGCAACCC
AGATGTCAATCTGCCAGGGAGATTACGAATCCATTAGACAAACAGGAACATCTCAGT
GCAAGGAGGAGCCATTGCCGGAAATAATTACGTCAAGGGTAACAATGACTCAATGTA
TAGCCAAGGACCAAGTCCTCCTATTCAAGTATTAACAAGAATATCGAAGGACCTACTGG
ATTCGATCATTCAAGGACTATGGGATCCAGAGGTAACTCTGCATGCTATTGAAAGCGA
TGATGATGAAAACCATTATTCAAGAGATTAATGCCGGTCTTCACTATCGAAGGACTGGA
TGAACAGGATAATGAGAACTCAATTATTAAACAACCAGGAAATCAGTGTACTGAGGGAGT
GTCTAAGACTGATTCACTCCTAGTTCCCAGGAAACTACACTATCTGTTGGGGATCTGA
TATACCTGGACAGGAATATCAACCTGTGCCCTTGGATATAACTGTAAATGAACTCGA
AGATGCAACTGTAAGAAATAGCAACAATATGAAAGGAACTGCCATTCTAAATTACT
AGTTAACGCCACCTAGGGTAAATCAAGTGTGATCACAGTAATCCAATTAAAGGGC
CACAGAAGGAAATTAGCCTCACCTGGGATGGAGACTACATTATCGAGAAGAGTGGTGC
AACCCCATCTGTACACCCATATACTCAACCTGCAAGCGACTTCAATGTAGGTGCAAGCAG
TGTCCATCAACCTGCCCTAAATGTGAATAATAATTGCAATGACGGTAGGGTAACAGCGCC
TAACTCACATAAGATATCGAGGGTAAGTCTGAAATATCTATTCAAGATATATAACTT
GATTCTGGATTAAAGGATGATTACAGGAAATTATCAAACAAATTAGATATGGTATTAGA
GATGAAACAAGACATTGACAATCTAAAAAGAATAGTGCTAAAGTGCATTAGCTCTATC
AACTATTGAGGGACATCTATCCAGTGTATGATTGCTATCCCTGGTTAGGTATTGATT
CACAGGGATGAGGAAAAGGACCAAGATAAATTCTGACTAAAACCACTGCTAGGAAGGGA
TCATTGTAGAGCATTGAGAACATTACCAATCCTAGATGAGTCTTCACTAGCCAATT
TCCAACAAAACATGTTGCCAAGGTAAACAAGAACTGCACACTTCAGAAGATCAACAAGAA
CGAAACATCTGCAATCAAATTGTTCTAGTGACAGTCATGCAAGCACATCAACCAC
GTCAATTATCAGGTCACTAATCTCGATCAGGATTGAAAACAAAATTGCTCACAATT
ATCCCAGATAAGAGGTGTAGACAATATTAGAGAATTCTATGAAAAGGTATGATATTAAT

Figure 3-3

AAAGAATAAGAATTAAATATTACAAATCTACATGCATTATAGTTGTAATTGTCTTCAAT
AAGATTGGTCAGTTCATATATATGGTTATTGATTGTGATAATTATAAAAAACTTAGG
AGCTAAAGATTACTCAGTCATATACAGCATGACTGAGATATTCAACCTTGATGAGAGCTC
ATGGTCAGTCAAAGGGACACTAGATCCGCTAACACCTGATAACCTATCCTGATGGTCGACT
AGTGCCTAAAGTCGAGTTATCGATCCGGTCTAGGAGATCGCAAGAGTGGGGGTATAT
GTATCTACTTCTTCATGGTGTCAAGAAGATAGTGAGACTATAATTAGTCCGAAGGAAG
AGCATTGGTGCATTCCCATTAGGAGTGGTCAATCAACTGAAAACCGGAAGACTTGTT
TAAGGAAATATTAACCTCAACATCGTACTCGTAGGACTGCTGGATTAAATGAGAAATT
GGTTTATTATAATACCACACCTCTACATTTACTGACCCCCCTGGAAGAAAGTGTGGCATA
TGGAGGCATTTTAATGCTAATCAGGTCTGCAGTGATACAAGTCCATACCAATAGACAT
TCCACAAAAATTAGGCCAGTATATTGACTGTTACAAAATTCTGATGATGGCTATTA
TCAGATCCAAAGATGATTCAAGATTCAAATCGTCAAATTCTGTTGCATTTAACATCCT
TGTGCATCTGTCATGGCACAAATTACTGACCAATCCAAGGACCCAGATTAAAGAAG
TGCTGCAGAAACTGTGATCACATTATGATTCAATTGAAACTTTAACCGGAAGAGTAA
TAAGTCTTACTCACCTGAATATTGCAAGAGGAAATAATGAGGCTTGGTTAATATTCTC
ATTAGGTGCAATTGGTGGCACAGCTGCATATTAGATGTACAGGTAAGATGAGCAAACG
ACTACAGGTTATTGGGATTCAAAGGACTTTATGTTACCCCTTGATGTATGTTAATGA
AGGGCTGAACAAGACCCGTGGAGAAATGAATGCAGAATAGAGAAGGTTCAAGCAGTCCT
ACAGCCATCAGTCCGAATGAGTTAAGATATATGATGATGTTATTGATAATACCAA
TGGTCTTCAAGATTAAATAGACTATAACAATAATAACGCCACCAATGGTACCATG
TATTCAAGTGTACACTGACAATTGCGAATAAAATACCAAGGTTAACACAGTATAGAGT
TAAGATCTAATTGATATGTGGTTGGTACTCGATCAATTAGCTACTGATTATCTA
TATCCTAAATACCAAATATAAGAGCATCAACAGGTAATAAGTTGGATTGCTAGATT
ATACTTAATTCTCAGAACTAGAATACACAGATTGTCAAACCTATAATCTGTTAGATTCA
TTAAAGTTAGATTCTGTAATGTTGATCAATTACTCGAGCAATTATAAAAAACTAAG
GACCTAATGTAATAGGAGCCAAATTCCATCCAGTGAGCTTAAATGCCATGCTTAAAC
ATTAATTGTCCAGGGCCTATCTAACTCAGAACAAAGATCACAACAGTCTGAAGGAG
TGGGTTAAGTCTGAATAATTATAAGAGTTGAGATTAAACTGATTCCCTTAAATT

Figure 3-4

AGAATTAAATAATATCATCCATTCAATATCATGAAACAGGATTAAAGGTTATAATAATT
AGTCTTTATTACTATCAGATATTACGATTGCCACAAATAGGTGGATAATTGACTTCG
ATTGGAGTTATAAGTACTAACGAAACAGACTATAAAATAACTACTCTGAACACTGACCAG
TTAATGGTTATAAAGATGGTCCTAATAATATCATCAATCATTAATTGCACTAAACTCGAA
TTAACAAAATACAGAGAGTTAGTCAGGGATCATTAGACCAATAATGAGTCATTAGAA
TTAATGAATTACATACATTAACATGAGAGCAGGTTCAGAGAGATTCAAGGGCTGTAATA
GCTGGTAGCCTAGGAGTGGCAACTGCAGCACAAATAACATCAGGGATTGCCCTACAT
AATTCAATTATGAACAAAAACAGATACAAGAATTGAGGAAGGCTTAGTACTACTAAC
AAAGCAATTGATGAAATAAGGATTGCAGGTGAAAGAACATTAATAGCAATTCAAGGTGTA
CAGGATTATTAATAATATAATTATCCCTATGCAGGACAAACTCCAATGTGATATTITA
TCATCACAACTTCTGTTGCTTACTCAGATATTACAAATATATTACAGTTTTGGG
CCAAGTATACTGGATCCTATTACTAGTACAGTTCACTACAGGCACTCAGTCAGCATT
AATGGTAATCTCAGGCATTGCTTGATGGATTGGATATACTGGAAAGACTTACGTGAT
CTTCTAGAGAGTAAATCTACTGGCCAGATAATTCACTGCAGATATGACTGATTGTT
CTTGTTCTGAGAATAAATTATCCTCTATAACTGAGATGCAGGGAGTAACAATATGGG
CTCAATTCAATTACATCATATTGGCCTGAAGAGTGGTATACCATTATGCCGATT
ATTGCTGTTAGGGTTTTAATATCTAATTGATGAGAGAAAGTGTCAATAACTAA
TCAAGTATATTGTGCCAACAAAATTCAATTACCAATGTCAACAGAGATGCAAAGATGT
ATTAAGGGCAAATAAGATCTGTCCAAGATCCAAGGCAATTGGACATTAGTCAATCGG
TTTATATTGACCAAAGGTAAATTGATGGCTAATTGTTAGGGATTATGCAGATGTTAT
ACTTCAGGCCAAGTTATAACACAAGACCTAGTAAATTGATCACGATAATATCGCAAGAG
GAGTGCAAGGAAGTTGGTGTGATGGTATCCGTATTATGGTAGGACCTAGAAAATTACCA
GATATTACCTTAACGCTAGGTTGGAAATTGGTGTACCGATATCATTAAGGCATTGTTAGAG
CAATCAGATAAGATTGGATTCAATGTCTAAATTGGATTCTATGAACTCAAGAATAATA
GGGTTAATCTTAGCAATTATGATAATCTTATAATCATTATTACTATTATCTGGATCATG
TATAAGAAATGTAAGAATAAAGATAATAAATTCACTGACTTCAATTGAACCGCTACATA
CCCCCTTCTATAACTCACCTCATAGTGTGGTAAATCTATTGAGTACTGACTATATGA

Figure 3-5

TCCACTGTAATAAGTCCAATGAAAGTATCAATTAAATAATATTGGTAGTGCAATAAGTATT
GATTGTATAATATACTCCTTAAACTAGATAGTAGATAAAGGGTTATAGATGATTCAGTC
ACTTTAATATAATCATATATTGGTTTATTATCTTGATAACTATTATGTAATTGAATTA
TGTATCATCAATTAAAGCTTAATAATATGTTTAATATACTTATATTGATAGATAAATG
TGTATATTGTAATCAAGGAGTTGGTATTAGAAGAGGAAAGAGTTAAATTGTTAA
TTAGTTATTGTGTATTCAATTAGAAAAAACTTAGGAATCCATGTTAATAGAAATTATTAA
TCATGGAGTCCAACAATATTAAGTACTACAAAGATTCTAGCCGGTACTTGGTAAAATAT
TAGATGAACACAAAACAATTAAATAGTCAATTACAGTTGAGTATCAAGGTAAATTACCA
TTATTGCTATTATTGTAAGCCTGATTGCAACAATAACTATTATCAATGCCACTAGTG
GGAGAACTACCCCTAAATAGTAATACAGACACTACTCAGCCAACGAGATGAGATTCAA
ACATCCAAGAAATGATATTGATCGTATTATCCTTGATAAAATGCTATGAGTACAGAGC
TAGGACTTCATATTCTACCTTAITGGATGAACTTACTAAAGCGATTGACCAGAAAATTA
AAATAATGCATCCTCCTGTGGACACTGTGACTTCTGACCTTAATTGGTCATCAAACCCC
CTAATGGAATTATCATAGACCCAAAAAGTTATTGTGAGAGTATGGAATTGTCTAAAACCTT
ATGAATTGTTACTTGACCAGTTAGATGTCICAAGAAAGAAATCACTTATTATAATAGAA
AGAATATTAACCAATGCCATTAGTGTATAATTCAAAGATCATTGCACTGTCAACAA
TACAATCTACACCGAGGTTTTAAACTTGGTCACACGGTCAGCAATCAACGTATAACAT
TTGGTCAGGAACATATAGTAGTACTTATGTTATAACTATCCAAGAAGATGGAGTAACG
ATGTTCAATATCGAGTGTGAGATCGGATATATTGTGATCAGTTGGTATTCCCT
CCTTAATAGTATCGAGAGTGTGCCGATACGCATGCTATTAGAAATGGAATCCTGTACCT
TGACAAGTGTAGACTAGGCAGGTATTTTATGTATGAATACACTGACACGATCTATAT
ACGATTATGTTAGCATAAGGGATTGAAATCACTTATATAACAATCCCTCATTATGGTA
AAGTTAATTATACTTACTTTAATTGGTAAGATCAGGAGCCCACATGAGATTGATAAAA
TTTGGTTAACATCTGATAGAGGCCAATTATCTCTGGTTATTTGAGCATTGTTACCA
TTACAATTCCGAACTATAATAATTATCCCTACAAATGCTAAATAACCCATGTTTGACA
ACTCTGAGAATTACTGTAGAGGGATGGTATAAAAACATAACAGGAACGTGATGATGTTCCGA
TATTAGCATACTTATTGGTTGAAATGTATGATGAAAGAGGGACCTTTAATTACACTGTGG
CAATACCACCTTACAATTATAACAGCTCCATCTCATAATTCTCTTACTATGATGACAAAG

Figure 3-6

TTAATAAAATTAATAATGACTACATCTCACATAGGTTATATTCAAATCAATGAGGTGCATG
AGGTAATTGTTGGCGATAATTGAAGGCTATCCTCTAAACAGATTATCTGATGAACATC
CTAACCTGACTGCCTGTAGACTCAATCAGGGTATTAAGGAGCAATACAAGTCGACGGAA
CAATAATTCAAATTCTGTACTTATTGATATAACAAGAACGAATGTACATTACAGTTAAAG
CTATTCCACCAGCAGGTAACTATAACTTACAGTTGAGTTGCATTCTAGATCAAACACAT
CTTATGTATCGTTGCCAAGACAGTTAATGCTAAGTATGACAAATTACATCTTGAGTGCT
TTAGCTGGACAAATCCTGGTGGTGTGCTCTGATACCTCAGTTTCATTAAGTTGGAATG
AATCCCTTCTGTTGATACTGCCATTTCATTAATAAGCTGTCAATGAACACATCAAT
CTATAGTTGATAGTTGTCAAAACATTAGCCAATTGGGTTAAAGAAATAGGAAAATGAAA
TTATCAATATCTAATTAGATGTATGTTCAAGCTAAATTACAAAAAAACTTAGGAGTCAGAG
ATTTCGTTGCAATGGAGCAGTCAGACTACCAAGATATTCTATACCCGGAAGTACATCTTA
ACAGTCCTATAGTAATTCCAATTAGTAGGTATTAGAATATGCCAAATTGGTCATA
ATCAACAATTATCAGACCGTACAATTATCAAGAATATTCAATTAGATTAAGGAACGGAT
TTAATAGTTCAAGGGTACAGGTACTATCAACTATGGGTGAAATTATCAACAAAATTAGAA
ATAAAATATCCTAATTACACATACCTTACCCCTGAATGCAACCAAAACTATTTCGAA
TAGTAGATCCAGAACTAACATCAAATTAGAATCTCTCTAAACAAAGGTGACACACTGT
ATCTCAAGATTCGATCAGATATCATAAAGTGTITGATAGATTGAAAATGAAAATGAACA
TAAAGAATGATCTCTCAATGACAATAGTCATTGATTCTAGATCTCCTTAATTATCA
AAGGATCTCAGTGGTCTCCCTTTTATTTGGTTCTATCAAACACTGAAACTAGAA
GCTGTATTGCCAAATCAAAGACTCGTGTAGATCACAATATCGGCCTCACTTATCAG
AGACTAAGAGAATTACATTGGTTGTTACATCTGATCTGATTACAATATTGATCATATTA
ATAAAATGTATATTATTGACTTTGAGATGCTGTTAATGTATTGCGATGTGATAGAAG
GTCGGTTAATGACTGAAACAGCTATGAGCTGGACTGTCGGTTACCAATCTATTGCCAA
GAGTGCAATATATGTGGGATTACTAGATGGAATGTTGAAAGTTAGGCAATCAATTAT
ATTCAAGTTATTGCATTATTAGAGCCTTTCTGCTTATTGCAATTGATAGATGCAG
ATCCACAGATTCGGGAACATTCCCTGCATCACTGCTTCCGAGTTAGAAGAAATTATAT
TTGACAAAACCCCTTGATCCTTCGTATATGAAAATTAAATTAAATGGACTTGATTACA
TTTATTGACAGATGATATTCAACTGCAGAAGTTTTCTTTAGAAGTTG

Figure 3-7

GTCATCCTTTAGAACACAAATGCTGCCAATAATGTAAGGAAGTATATGAATAAAC
CTAAGGTAAATCTCATATCAGACTTAATGCAAGGACATGCGATTTTGCAGTATTATAA
TAAATGGATTAGAGATGCCACGGGGAACATGCCCTCTGTAGAGTACCAAATCATG
CATCTGCTGTAATTAGAAATGCCAGTTATCTGGAGAAGGGTAACATCTGAACAATGTG
CTCAACACTGGAGATCCTCTGTGGATTAGTTAAATGTTATGCCATTGAGTCTAG
ACAGTGACCTTACAATGTACCTTAGAGACAAGGCGTTACCTGTCAGAAATGAGTGGG
ATTCAAGTTATGCTAAGGAGTATTAAAGATATAATCCAGGATTACCCACAAGTTCCAGAA
GATTGGTAAATGTATTCTAGAAGATGATAAGTTGATCCATATGAAATGATCATGTACG
TGATAAAATGGTGATTACTTAAGAGACAAAGAGTTAACCTTCATACAGCCTAAAGAGA
AAGAAAATTAAAGAGGTAGGTCATTGTCGCTAAATGACCTATAAAATGAGGGCTTGT
AAGTAATAGCTGAAAACCTGATTGCCAATGGAGTAGGGAAGTTTCAAAGATAATGGAA
TGGCAAAAGATGAACATAAATTAACTAAAACGTTACACAAATTAGCCATTCAAGGTGTAC
CTAAAGATAATTCTCAACTTATTAGATGAATGTTGGAGCAAGTAATTGACAATGTT
CAAGTAGTACACAGATAAGGAAACAGGCTATGAATTACAATCAAATAGGGAAATTGAAT
CAAAGTCTCTAGGGCACGTCTAATAATAGAGATATCTAAAGGGCAAGAGAGATTGCA
ACAAACAAATAAAAGTATCCTTCAAACACCAGTATTATGAGACTATCAGTAGTTCTAA
CTACTGACCTTAAAGTATTGTCCTAACTGGCGATATGAATCAAGTAGTAGTGTATTGCA
AGAGACTTAATGAGATTATGGACTGCCTGGATTTCAGTGGCTTCACAAGATTTGG
AGAAATCTGTTCTACGTTACTGATCCATATAGTCCACCTGACTTTGATCAACATATCG
ATATAGAATCAGTCCAAACGACCATACTTATCAAGTACCCGATGGGTGGAATAGAGG
GGTTCTGTCAAAATTATGGACCATTAGTACAATTCCGTTCTATATTAGCAGCTTTG
ATACAGGGTTAGAATCTCATCATTAGTCAAGGCGATAACCAGGCAATTGCACTGACCA
AAAGAGTTCCGTACCTGGAGTTATTCAAAGAAAAGGAAGAATCAACTAAATAACAA
CACAGTATTCTTAATTAAAGACAACGCTTACACGACATAGGTATGAATTGAAAGCAA
ATGAGACTATTATATCCTCTCATTCTTGTACTCTAAAGGTATTATTATGATGGAA
TACTTCTCTCCCAGGCACCTAAAGTATTGCAAGATGTGTCTTCTGGCTGAAACGATTG
TTGATGAGACTAGGTCACTGCAGTAACATATCTACGACACTCGCAAAGGCAATTGAAA
GGGGTTATGATAAAATTGTGGCGTACGCTATCAATATTATAAAACAATACATCAGGTGT

Figure 3-8

TGATTGCATTGCCTTACGATTAATCCTACTATGACACCAGACATCACAGAACCTTTCT
ACAAGAGTTAGATCTACTTAAGAATCTAGCCTGATTCCCTGCACCATTAGGGGGCATGA
ACTATATGAACATGAGCAGGTATTTGTTAGGAATATAGGAGATCCCATTACTGCTTCAT
TTGCTGATATAAAGCGCATGATTGAATGTGGGTGTTAGGATGTAGTATTCTGTCACAAA
TAATGTACCAAAATGTGGTTCCCTAAATACCTAGACTGGGCTAGTGATCCTTATTCAA
TAAACCTTCCTTATAGCCAAAGTATGACCAAGGTTAAAAATGTAACGGCAAGATATG
TACTTATGCATAGTCCCAACCCTATGCTCAAAGATTGTTCCATGAAAAGTCTCAGGAAG
AAGATGAAATCCTTGCTGAGTTCTGTTAGACCGACACTTAATAATCCCTAGAGCAGCAC
ACGAAATTTATCAAATTCACTAGTAACAGGTGCTAGAGAATCTATAGCAGGTATGCTTGACA
CTACTAAGGGTTAACCGTGCTAGTATGTCAAGAGGTGGGTGACCTCATCACITGTTT
TAAAATTATCAACATATGATTACCAACAGTTAGAACATGTCTGAATGGCTTATGCTC
CTACTACGGGAATTGCTGTAAGCGTTGATTCTGCTCTGTATTCTTAGCTAACGACATCC
GGAAGAGAATGTGGGTTACCTAACTAAAGGAAGGGAGATTATGGGTTAGAAGTACCTG
ACATTGGAAATGTATGCAAAACAATATTATTGTTGATCACGAAGATTGTTACTCATGTA
TTCAAGGATCAAGATATTATACATGGTTTTGTACCTTCAAATTGTCAACTCGATCAAA
TAAATAAGTCAACAAATTCTCTCCGAGTACCTTATGTTGGATCAACAACTGAAGAAAGGA
GTGATATGAAGTTGTCATATGTAAGGTACCTAGTCGCCACTTAAAGCAGCAGTTAGGA
TTGCAGCAGTATATACATGGCTTATGGTGTGATAATTGTTGGCATGAAGCTTGGT
ATTTAGCAAGGACTAGAGCAAATATTACTTTGACGAACCTAAATAACACCTATAG
CTACATCTACAAACTTACGACATAGATTGAGGGATAGAACGCACACTCAAGTAAATATTCA
GAACCTCTTAGTAAGAGTGGCACGCTATACAACAATATCTAATGATAATATGTCGTTCA
TTATTAATAACAAGAAAGTCGATACTAATTGTTGCTACAGCAAGGAATGTTATTAGGTT
TGAGTATATTGGAATACATATTCACTAGACTGTACAAGTACTGGACAGTCAAACACTGTAA
TTCACCTACATGCAGATGTTAATTGTTGTTAGTACAGATGACTGATCAGCCTTACAC
CAAGTTAACAAAAAGCTACCTGATATTAGCCCATTAAATAAAACTGATATATGATC
CGGCTCCTATAATCGATACTGATGCAGCTAGGCTATATTCCAAAAGTACCTGTCACATT
TAATAGATTTCCAAGTTGGTCAACTACTCAGCTAACACAGTATTGGCGAAAGTAGTGG
CGGTATCTATTGGAATTAAATTACAAAGCGAGTAAAGACCACCTCAATGAGATAATAG

Figure 3-9

CAGTTGTTGGTGATGATGATATCAATAGCTTATTACAGAATTCTACTTGTGATCCAC
GTCTGTTACACTATTTAGGCCAATACACATCATTACAATGGGCATATGAAGTCATT
ATCATAGACCAGTGGTAAATACCAGATGGCTGAAGTGTGCATAATTGCTGTCAAGAG
CTAGTAGAGGTATTCAGTATTGACCAATGCCTTAGCCACCCAGAGTCTACAAAAA
GATTCTGGGAGTGTGGTTATTGGAGCCTATTATGGCCCTATATAGGAAGTCAAAATC
TACATAATGCAATGATTGATTATCTATAATGCATACATTACTTATTGGATGCTTATT
TATCTGATCAAGTAGATGATACTGATATTATAATATGTGAAACAGAGGAGACATGTTGG
CGAACATCGAACATTCAAAGCAGACACTTAGCTGTGCTTATAGATCTGTATTGTG
ATTCCACTAGATGTCCCATAAAAAGGGCAGATACAATTATGAGAAATTCAATTCTTA
GATCTTCATGATAATGAGAGGAGAACAAATCCACTTGGTTGACATGGAACCTTGACC
CGTTACTTGTGOGATCACTTAGCTGTCTATTACGTATCTGAGGGAGAGGTATTAAAC
AGATGAGGTTAAGATTGATCCAAGTGTATCGCTGGAACATCTAGGATGATTAACCTG
ATGCGGTTATCAAGCACCTAAATTCCGCTTCATGGCCTTATAGATATCAACCTG
AAGTAAATGACCTTAATGTAATTGGAGAGCTGAATAGCAAGTGGAAAGATATCCCTA
TTGGACAGATTAGAATACAGAATTATGAAATACATGCATATAGGAGGATTGGAGTTAATT
CAACTGCCTGTTATAAGCTCTAGAGCTATATCTGTTCTAAATCGGTTATGCCTAATC
CATCAGGTGCATTGTTTAGGTGAAGGAGCAGGATCAATGCTGGTCACATACCGTGCTT
TTGTCCCATTAAAGACAATTATTACAATAGTGGTATTCAGTCAAAATGTTAGGGCC
AGAGAGAATTGAGTCTATATCCATCTGAAGTGGCACTAGTTGACAACACAAAATCGCTTGG
CTAATGACCTAATATCAAAGCTTGTCAATGGTAAGCCAGAGTCTACGTGGTTGGAA
ACATCGACTGTTTGCTTATATTCTAGCCACATTGAGACCTCAAGCTGACATTGATAC
ATAGTGATATTGAGTCCAGCTTAAGCAAGACGAAGAATAAAATTCTTGAGGGAGCTGTGCC
ACATTCTGTCAATGGCACTCATTGGGGAAAATCGGATCTTATTAGTTAGGTAAAGTTAT
TACCAAGGGTGGTGACTACGTATTCTAGGTATGCATCGGAATTCTATCAAC
AAAGCCTCCTGTTACCTAGGTTAGTAACATGTCATCTGAGGTTACTATATAG
GAATTCACCTCAATACAAATCGATTGATTGATCTGATAGAATAGTACAATACATAATT
GAAATTACAACCAACTCCAGTTACATTGTCTTATTTGAAACTAAGTATAGGA
ATAATATGGTTACAAATTATGGACTGTGCTTGAGACGGACACAAAAGTGATTACCTGT

Figure 3-10

CATCAATTACAAAAATAGAGAATGTTCTCCTGTATGTGGGTTAGAATTGAATGGACCTA
AGATTATAACAGCAATTATCAGGACATGACTATGCTAATGGGGAGACTAGTCTAGAACCAA
GTATAATGATATTAGITAGGAAATATCITAATGCAACTATACAGGGCCGGGAAACATTAG
GCTTGTTCACCTTACCCAGTCTTACATGAGAGTCAGTTAAGAGAGATTAATAAGTGA
TTGCATTGAAATAATGTTGTATACTCTTTATTCAAACCTACATTATCTAGTAAAC
AAATAATGAGTAATCTCAGAAAGGAAATTGATGTATGATTGAGAGATGAATTTCAT
TATCAAGATTGTCAGCAAATTACAAGAAAAAGGTGATGTCACAGGAAGTCAGACTACCT
GGATCTTAATATTGATACTCCGACACGAAAAGCATTATATAAGTTAGTAGGTTATTCA
TAATAATTAAATCATGTATGATGATAGAGTGTGATTATCCATCTTTAGAGAGTAAGATAA
TATCAGATGTATGATAACCAATTAAAGTATTGCTTGAATTGAAAGGTTGCTCAATTACA
CGCTTCTTAGTAATCGGGTTTTATTCCAATTAAAGCAATTAGAAAAAAACTCAACAGT
TAGTCGAGCCCCGAATTCAATTACATAAGTTATTTATAATCTGGATAAGACTTTGT
TTAGAATTATAACAGTAATACTAATTATGAATGGAAGACAATTGATATCTAGTGTGAAT
TTICATGCTTATGTGTCTTAACCTTAACTCACGATCATTCTTTATTGAGAATTAA
ATTATAAGGTGTTATGTGTGATGGGAACCCTCAATGCTGACATTATTAAATAACCA
TAGGTATTGTATGAGATAATGTTATTTACCAATGTACAATCTCATATGTCGGACCC
CTTAACCTCCTCCTTATAGTTGAGTTCTGGAAAAACACAAAGATGATCTTGAGTAAT
TGTACGGACCTATAGCTTCTTGTCTGGT

Figure 4-1

FmoPV M252A Cats/China/2010 16050 bp

ACCAAGACAAAGATGTCTGTGACCTATTCTAACGACAAGACTATTATAAATATTTAGGAA
TAACGATTCCATTAGTGGGTGAGGGGAAGGAATCAGGTATTCCAGAATGTCGAGTCTAC
TGAAGTCACITGCCGCATTAAAAGACATAGAGAGCAACCAACTACACCGTCAGGTTCA
GTGGTACAATTAAAGGATTGAAAAACACAATTATTGTTCCAGTACCAGGGATACAGTAA
TTACCACGAGGTCTAATTGTTATTAGATTAGTTATATAATAGGCAATCCAGATAACGC
CTCTAACGACCTCGACGGGAGCAATAATATCATTATTGACCTATTGTCGAATCCCCAG
GTCAATTAAATTCAAAGAATTGCCGATGACCCCTGATGCAGTTTAAATTAGTAGAGGTCA
TTCCTGAAGCTGGTAATCCTGGAGAATTGACTTTGCATCTCGAGGGATTAATTAGATA
AGCAAGCCCACAATACTTAAACTGGCTGAGAGAAATGATCAGGGTATTATGTTAGCT
TAGGATTGAGAACCCACCAACGATGATGATAACATCTAGCCTGAGATAATTAAATT
ATATTGGCATCTGTACTTGCGCAAGTTGGATTCTCTGGAAAAGCTGTGACTGCTC
CGGATACAGCTGCTGAAGCTGAAAACCGTAGATGGATTAAATTGATGCAACACGTCGG
TGGATGGTAATTAAAGATTGAGTAAAGGATGGCTAGATTGGTAGAAATAAAATTGCGT
CAGATATTACAATAAGACGATTATGGTGGCATTAGCCTTGACATCAAACGTTCTCCTG
GGACAAGACCCAGAATAGCTGAAATGATTGTGATATTGATAATTATATTGTAGAGGCAG
GGCTTGCAAGTTCTGTTAACTATTAAATTGGCATAGAGACACGTTATCCAGCATTGG
CATTGCATGAGTTCTGGAGAATTAGCTACTATTGAGGGACTTATGAAATTGTACCAAT
CTATGGAGAAATGGCACCATATATGTAATTCTGGAAAATTCAATTCAAACCAGGTTA
GTGCCGGTCTTATCCTTGCTATGGAGTTATGCCATGGCGTGGTGTGGAGCTTGA
GATCGATGGTGGACTTAATTACTAGGAGCTTCTTGACCCCTACGTACTTCAGACTTG
GTCAAGAGATGGTGAGAAGATCTCAGGGATGGTAATAGTCATTGCGCGAGAACCTG
GGCTATCTGAACATGAGACACAACTTGTCAAGCCAATTGTAATTGGAGGAGGTGAATCTG
GGATAACCTAAATTGATGGATTCAAGAGCAAATCCAACAAACCTTCTAGGAACCAAGATA
ATATTAATGATAAAGGTGAGGATCAGTCAAGTTCACTATCAGGGTTACCTGGTCCATTAT
TACCCAGTCGTGACCTAACTCATCCAGGTGATTCATGGAGCAGATGATGGTGTGAAAA
ATGTCAGTAATAAATTGAGTGAAGGAATAAGTCCAGATCATGATGTGTCTAGCTGCCA

Figure 4-2

TGGAAGAATTGAGGAGGTTAGTTGAGTCTACCAACAGAATTGACACCAAAAAGCCCGAAG
CTCCAGGTGTCACCAACCATTATAATGACACCGACCTTTAAGATAATATGAGTATATCT
TATTTGATCATCATAACAATTCAAATTAAGAAAAACTAGGACCTCAAGGTTACAACGT
TGGCACATCACTGAGATATAGTCAATTCTTACCCACCACATGTCCTCTCACCAAGATTCA
ACAAGTCAAACATGGCCTCGAACATCTTACAAGAGATCAAAAACAACCCTCCGTCTTCAA
AGATGTCGATCTGCCAGGGAGATTACGAATCCATTAGACAAACAGGAACATCTTCAGT
GCAAGGAGGAGGCCATTGCCAGGGAGATAATATTACGTCAAGGGGTAAACAATCACTCAATGCA
TAGCCAAGGACCAAGTTCTCCTATTCAAGTGTAAACAAGAATATCGAAGGATCTACTGG
ATTGATCATTCAAGGACTATGGGATTCAAGAGGTAAACCTCTGCATGTTATCGAAAGCGA
TGATGATGAAAACCATTATTCAAGAGATTAATGCCGGTCTCCGCTATCGAAGGATTGGA
TGAACAGGATACTGAGAACTCAATTATTAAACAACCAGGAAATCAGTGTACTGAGGGAGT
GTCTAAGACTAATTCAACCTCTAGTCCCCAGGAAACTACACTATCTGTTGGGGATCTAA
TATACCTGGACAGGAATATCAACCTGTGCCTTTGGATATAACTGTAAATGAACATTGA
GGATGCAACTATAAGAACAGCGACAATATGAAGGGAAACTGCCAATTCCGAAATTACT
TGTTAACCGCCACCTAGGGCAAGATCAAGCATTGATCATAGCAATCCATTAAAAGGGC
CACAGGAGGGAAATTAGTCTCACCTGGGATGGAGACTACATTATTCAAGAGAGTGGTGC
AACCTATCTGTACACCCATCTACTCAACCTGCAAGCGACTTCAATGTAAATGTAAGCAA
TGTCCATCAACCTGCCCAAGTGTGAATAATGATTACAGAGACAGTGAGGTAACAGTGCT
TAACCTACATAAGATATTGAGGATAAGTCTGAAATATCTATACAGGATATATAACTT
GATTCTGGATTTAAGGATGATTAGGAAATTATTAACAAATTAGATATGGTATTAGA
GATGAAACAAGACATTGACAATCTAAAAAGAGTAGTGCTAAGGTACAATTGGCATTGTC
AACTATTGAAGGACATCTATCTAGTGTATGATTGCCATCCCTGGTCAGGTATTGATTC
CACTGGGAAGAGAAAAAGGATCAGATGAATTCTGACTTAAAACCATTATTAGGGAGGGA
TCATTGTAGAGCATTGAGAAGTTACTAACCTCTAGATGAGTCGTTACTGCCAATT
TCCAACAAAACATGTTGCCAAATAGACAAGAATTGCACTCTCAGAAAATCAACAGAA
TGAAACATCTGCAATCAAGTTGTTCCCAATGATAGTCATGCAAGCACATCGACCACCAA
ATCAATTATCAGGTCACTAAATCTCGATCAGGATTGAAGACAAAATTGCTCACAATTCT
ATCCCAAATTAGAGGGACAGAGAATGTTAAGAATTGAGAAGGTGATGATATTGAT

Figure 4-3

AAAGAATAAGAACTAAATCACCAATCTACATGCACTATGAGTTGAATTGTCTTCAGT
AGAATTAGTTGATTAAATACATACTGTTGATITGTAATAATTATAAAAAACTTAGG
AGCTAAAGGCTACTCAGTCATATACAACATGACTGAGATATTCACTCTGATGAGAGCTC
ATGGTCAATCAAAGGAACACTTGATCCGCTAACACCTGATATCTATCCTGATGGGAGACT
CGTCCCCAAAGTCGGGTTATCGATCCGGGCCTAGGAGATCGCAAGAGTGGGGATATAT
GTATCTACTTCTCCATGGTGTCAAGAACAGCGAGAACATGATTAGTCCAAGGGGAG
AGCATTGGGCATTCCCATTAGGAGTGGGCAATCAACTGAAAACCCAGAAGATTGTT
TAAGGAAATATTAACTCTCAATATCGTACTCGTAGAACTGCTGGATTAAATGAGAAGTT
AGTTTATTATAATACCACACCTATACATTACTGACCCCCCTGGAAAAAGGTGTTGGCATA
TGGAAAGCATTTAATGCTAATCAGGTCTGCAGTGATACAAGCTCTACCAATAGATAT
TCCACAAAAGTTAGACCTGTATATTGACTGTTACAAATTATCTGATGATGGCTATT
TCAGATAACCAAAAGATGATTCAAGATTCAAATCGCAAATTCTGTTGCATTCAACATCCT
TGTGCATCTATCAATGGTACAAATTACTGACCAATCCAAGACTCTCGATTAAGAAA
TGCTGGGAAACTGTGATTACATTATGATTCAATTGGAACTTCAAACGGAAGAGTAA
TAAATCTTATTCAAGCGGAACTGCAAGAGGAAAATAATGAGGCTTGGTTGATATTCTC
ATTAGGTGCAATTGGTGGCACAAGCTTACATATTAGATGCACAGGTAAAGATGAGCAAACG
ACTACAGGCCTACTTAGGATTCAAAGGACTTTATGTTACCCCTGATGTATGTAATGA
AGGGCTAAATAAAACACTGTGGAGAAATGAATGTAGAATAGAGAAGGTTCAAGCAGTCTT
ACAGCCATCTGTTCAAATGAATTAAAGGTATATGATGATGTCATTATTGACAATACCAA
TGGTCTCTCAAGATTAAATAGGTATAACCGTAACAAACAGCTAATAATGGTATTATG
TATTAAAGTGTACACTGATAATTGTGAATAAAATACATTGGGTTAATAACGGTATAGAGT
TAAAATCTAATTGATATGTGGGTTAATGCTTAAACACTTATTAGCTCTATTGATTATCTA
TATCTTGAGTTATCTAATATCAGAGTATCAACATGTAATCAGTTAAACTTGTGGATT
ACGTTCAATTATAACCAGAACACAAATTGTTAAACTTATAATTCTGTTAGATTCA
TTCAAGTTGAACCTATGTAGGGTTAACCAATTATCATTGAGCAATTATAAAAAACTAAG
GATCTAATGTAGTAGGAACCTAAACTCCATCCAGTGAGCTAAACACTCAAAT
ATCAATTGTCTAGGGCCTGTCTAACTCAAAACAAAGCTCATAACCAGGATCCAGACGAG
TGGGTTAAATCTGAATAACTATTAGGAATTGAGATTAAATTGATTCTCTCTTAACCTCT

Figure 4-4

AAAGTTTAGTAATATAGCATCAATT CAGCACC ATGAACAGAATTAAAGTTATAATAATT
AGTTCTTGT TATTATCAGATATTACGATTGCACAAATAGGCTGGATAATTAACTTCG
ATTGGGTTATAAGTACTAACGAGTACAAC TAACTACTCTAAATACTAACTAAC
TTGATGGTTATAAGATGGTCCCAATATATCGTCAATCATTAATTGCAC TAAACTTGAA
TTGATAAAATATAGAGAGTTAGTCTCAGGGATCATTAGACCAATAATGAGTCATTAGAA
TTAATGAAC TACATACATTAATATGAGAGTAGGTTAGAGAGATTATAGGGCTGTAATA
GCTGGAGTAGCATTAGGAGTGGCAACTGCAGCACAAATAACATCAGGGATTGCCCTACAT
AATTCAATTATGAACAAAAAACAGATAACAAGAGTTGAGGAAGGCTTTAGTACTACCAAC
AAAGCAATTGATGAAATAAGGATTGCAGGTGAACGAACATTAATGGCAGTACAAGGTGA
CAGGATTATCAATAATATAATTGTCCTATGCAGGACAAACTCCAATGTGATATT
TCATCACAGCTTCTGTTGCATTACTCAGATATTACAAATATTAACAGTCTTGG
CCAAGTATACGAGATCCTATCACTAGCAGATT CGTACAAGC ACTTAGTCAAGCATT
AATGGTAATCTCAGGC ACTACTTGACGGACTAGGATAACTGGAGAGACTTACATGAC
CTTCTAGAGAGTAAATCTATCACTGGTCAGATAATT CATGCAGATATGACTGATTGTC
CTTGTCTGAGAATTAAATTACCCCTCCATAACTGAGATGCAGGGAGTAACAATATGAA
CTGAATTCAATTACATATCATATTGGCCTGAAGAGTGGTATACTATTATGCCTGATT
ATAGCTGTTAGGGTTTTTAATATCTAATTGATGAAAGAAAGTGTCAATAACTAAA
TCGAGTGTAAATGCCAACAAAATTCAATTACCCGATGTCAGCAGAGATGCAAAGATGT
ATTAAGGGCGAAATAAGATTCTGTCAGATCTAAGGCAATTGGACGTTAGTTAACCG
TTCATATTGACCAAGGTAAATTAAATGGCTAATTGTCGGATTATATGCAGATGTT
ACCTCAGGCCAAGTTATAACACAGGACCCAGTAAGTTAATTACAATAATCACAAGAG
GAGTGCAAAGAAGTCGGTGTGATGGTATCCGTATTATGGTAGGACCTAGAAAATTACCA
GATATTACCTTAATGCTAGGTTAGAAATTGGTGTACCGATATCATTAAGCAAATTAGAT
GTCGGAAATGATTAGCAATTGCTTCAGCTAACGCTAATAATTCCAAAGCATTGTTAGAG
CAATCAGATAAGATTCTGGGTTCTATGTCTAACGTTGGATTCTATTAAATTCAAGAATTATA
GGATTAATCTTAGCAATCATGATAATTCTTATAATTATGTTACCAATTCTGGATCATA
TATAAAAATTGTAGAAATAAGATACTAAATTCAAGTACTTCAATTGAACCGCTACATA
CCCCCTTATAACTCACCTCATAGTGTGGTCAAGTCTATTGAGTACTGACCATATGA

Figure 4-5

TTTACTGTAATAAGTCCAGTGGAAAGTATCAATTGACAATACTGGTAGTATAATGAATATT
GAATATATAATATACTCTCTAAATTGGATAGTGATAAAGAGTTAGATGATTGCAATC
ATTTAATATAATTATATATTGATTGATTACCTGGTATAATTCTTATGCAATTGAATT
TGTGTCATCAATTAATAGCTTAATAGCACTGTTTACACTTATGTTGATAGATAGATG
TGTTATATTGTAATCAAGGAATTAGTATCTAGAACAGGAAAGAGTTCAATTGGTTAA
TTGGTTATTGTTATTCAATTAGAAAAAACTTAGGAATCCATGTTAATAAAAACATTA
TCATGGAGTCCAATAATGTTAAATATTACAAGGATTCTAACCGATACTTGGTAAATAT
TAGATGAACACAAAACAATTAAATAGTCAATTGTACAGCTTAAGTATTAAAGTAATTACCA
TTATTGCCATAATTGTAAGCCTAATTGCAACAATAATGACTATTATTAAATGCCACAAGTG
GGAGGACTGCCCTAACAGTAATACAGACATACTGCTAGCCAAAGAGATGAGATTCTATA
ATATCCAAGAAATGATAATTGATCGTATTCTCCTTGATAATGCTATGAGTACAGAGT
TAGGACTTCATATTCCCTACCTTATTGGATGAACCTACTAAAGCGATTGACCAAAAGATTA
AAATAATGAATCCCCCTATTGACACTGTGACGTCTGATCTTAATTGGTCATCAAACCCC
CTAACGGAATTATTATAGACCGAAGGGTTATTGTGAGAGTATGGAATTGCTAAACCTT
ATAAATTACTACTTGACCAATTAGATGTCTTAAGAAAGAAATCACTCATTATAATAGAA
AGAATATTAAACCAGTGTCAATTAGTTGATGATTCAAAGATCATTGCTACTGTCAACA
TACAATCTACACCGAGGGTTTGAAATTGGTCACACAGTCAGCAATCAACGTATAACAT
TTGGTCAGGAACATATAGTAGTACTTATGTTATAACTATCCAAGAAGATGGATAACTG
ATGTTCAATATCGAGTTTGAAATCGGGTATATCTCTGATCAGTTGGTCTTCCCT
CTTAATAGTATCCAGAGTGTGCTACCGCATGCTATTAGGAATGGAATCCTGTACCT
TGACAAGTGACAGACTAGGTGGTATTCTGTATGAATAACACTGACACGATCTATAT
ATGATTATGTTAGCATAAGGGATTGAAATCATTATATAACACTCCCTCATTATGTA
AGGTTAATTATACTTACTTTGATTGGTAAGATCAGAACGCCACATGAAATAGATAAAA
TTGGTTAACATCTGAGAGGGGCAAATTATTCGGTTATTGCAAGCATTGTTACCA
TTACAATTCGAATTATAATTACCGCTACAAATGTTAAATAATCCATGCTTGACA
ACTCTGAGAATTACTGTAGAGGGGGTATAAAAACATAACAGGTACTGACGATGTTCCGA
TATTAGCATAACCTATTAGTTGAAATGTATGATGAAGAAGGACCTTAATTACACTTGAG
CAATCCCCGCTTACAATTATAACAGCTCCATCTCATAATTCTCTTACTATGATGATAAAA

Figure 4-6

TCAATAAATTGATAATGACTACATCTCACATAGGTATTCAGTTAATGAGGTGCATG
AGGTGATTGTTGGCGATAATTAAAGGCTATCCTCCTAACAGATTATCTGATGAACATC
CTAATCTTACTGCCTGTAGACTCAATCAGGGCATTAAGGAGCAGTACAGGTCTGACGGAA
CAATAATTCAAATTCTGCACTTATTGATATACAAGAACGGATGTATATTACAATTAAAG
CTGTTCCACCAGTGGTAACTATAACTTTACAGTTGAATTGCATTCTAGATCAAACACAT
CTTATCTATTGTTACCAAAACAGTTAATGCTAAATACGACAAATTACATCTTGAGTGCT
TTAGCTGGACAAATCTGGTGGTGCCTGATACCTCAGTTTCATTAAGTTGGAATG
AATCCCCTTCTGTTGATACTGCTATTAAATTAAAGTTGAAATGAATATGTCAAC
TGATAGTTGATAGTTGTCAAAACATCAGCTAATTGAGATTAAAGAAATAAAAAATGAAA
TTATCAAGATTGACTAGATGTACTCAAGCTAAATTACAAAAACTTAGGAGTCAGAG
ACTTCGTTGCAATGGAGCAGTCAGACTACCAAGATATTCTATATCCTGAGGTACATCTTA
ACAGTCCTATAGTAATCTCTAAATTAGTAGGTATTAGAATATGCCGAATTGCTCACA
ATCAACAACTATCAGACCATAACAATTCAAGAATATTCAATTAGATTAAAGAAATGGCT
TTAATAGTCCAAGGATACAGACACTATCAACTATGGGTGAAATCATCAACAAAATTAAAA
GCAAACACCCCAATTATTACACATACCTTACCCGAATGTAACCAAAAGCTATTGCAA
TAGTAGATCCAGAACTGACATCAAATTGGAATCTCTCTGAACAAAGGTGATAACTGT
ATCTCAAAATTGGTCAGATATCATAAAATGCTTGATAGATTGAAATGAAGATGAACA
TAAGGAATGATCTCTTAATGACAATAGTCATTAAATTCTGGATCTCCTTAATTCTCA
AAGGATCTCAGTGGTCTTCCCCTTTTATTGGTTTCGATTAAGACTGAGACTAGAA
GCTGTATCCGACAAAATCAAAAAGCTCGTGTAGATCACAATATCGGCCTCACTTATCAG
AGACTAAGAGAATTACATTGGTTGTTACATCTGATCTAATTACGATATTGATCATATTA
ATAAAATGTATTTATCTGACTTTGAGATGTTGTAATGTTGCGATGTGGTAGAAG
GTAGATTAATGACTGAAACAGCTATGAGCTTGGATTGTCGATTTATCAATCTATTGCCAA
GAGTGCAATATGTGGGATTGCTAGATGGAATGTTGAAAGTTAGGTAATCAATTAT
ATTCACTTATTGCAATTGTTAGAGCCTTTCTCTGCTTATTGCAATTAAAGATGCAG
ATCCACAGATTGGGGAACATTCTGCATCACTGTTTCAGAGTTAGAAGAAATTATAT
TTGACAAGTCTCCTTTGATCCTTGTGTATGAAATTTAATTAAATGGACTAGATTATA
TTTATTGACAGATGATATTCAACTGCAGAAGTTTTCTTTAGGAGCTTG

Figure 4-7

GTCATCCCTTTAGAAGCACAAATGCTGCTAATAATGTGAGGAAGTATATGAATAAGC
CTAAAGTGATCTCATACCAGACTCTAATGCAAGGACATGCGATTCTGTGGTATTATAA
TAAATGGATTAGAGATGCCATGGGGAACATGCCCTCTGTAGAGTTACCAAATCATG
CATCTGCTGTAATTAGAAATGCCAGCTATCTGGAGAAGGGTTAACATCTGAACAATGTG
CTCAACACTGGAGATCCTTTGTGGATTAAATTAAATGTTATGCCACTGAGTCTAG
ATAGTGACCTTACAATGTACCTCGGGACAAGGCCTGTACCTGTCAAAAGTGAGTGGG
ATTCTGTTATGCGAAAGAGTATTAAAGATAACAATCCAGGATTACCTACAAGCTCTAGAA
GACTAGTGAATGTATTCTTAGAAGATGATAAGTTGATCCATATGAAATGATCATGTACG
TGATAAAATGGTATTACTTAAGAGACAAAGAGTTAATCTTCATACAGTCTAAAGAGA
AAGAGATCAAAGAGGTAGGTGATTGTCGATTCGCCAAAATGACTTATAAAATGAGGGCTTGC
AAGTAATAGCTGAAAACCTGATTGCCAATGGAGTAGGGAAGTTCTCAAAGATAATGGAA
TGGCAAAAGATGAACATAAACTAACTAAACGTTACACAAATTAGCCATTCAAGGTGTAC
CTAAAGATAATTCTCAACTTATTAGATGAATGCTGGAGCAAGTAGTCGACAATGCT
CAAGTAGTACACAGATAGGAGAACAGACTATGAATTACAATCGAAGAGGGCAATTGAAT
CAAAGTCTCTAGATCACATCGAATAATAGGGATATCTTAAGGGCAGGAGAGATTGA
ATAAACAGATAAAAGTACCCCTCCAACACCCGAGTATTAGGAGACTATTAGTAGTTCATAA
CTACTGACCTTAAAAGTACTGTCTTAATTGGCGATATGAATCAAGTAGTGTGTTGCAG
AGAGACTTAATGAAATTATGATTGCGCTGGGTTTTCACTGGCTTCACAAAATATTGG
AGAAATCTGTTTATACGTTAGCGATCCGTCTAGTCCACCTGATTGATCGACATATCG
ATATAGAATCAGTCCGAATGACCATATCTTATTAAAGTACCCGATGGGTGGAATAGAGG
GGTTCTGTCAAAATTATGGACTATTAGTACGATTCCATTCTATATTAGCAGCTTGT
ATACAGGAGTTAGAATCTCATCATTGGTCAGGGCGATAATCAGGCAATTGCAGTGACCA
AAAGAGTTCCATCATCTGGAGTTACTCAAAGAAAAAGGAAGAATCAACTAAATAACAA
CACAAATTTCTTAATTAAAGACAACGCTTACACGACATAGGTATGAATTAAAGCAA
ATGAGACTATTATCCTCTCATTTCTTGTACTCTAAAGGTATTACGATGGAA
TACTTCTCTCAAGCACTAAAAGTATTGCAAGATGTGTTTTGGTCTGAAACAATTG
TTGATGAAACTAGATCAGCTGCAGTAATATCTACGACACTGCAAAGGCAATTGAAA
GGGGTTATGATAAATTGTGGCATATGCTATTAAATTTATAAAACAATACATCAAGTTT

Figure 4-8

TGATTGCATTATCTTTACGATTAATCCTACTATGACACCAGACATTACAGAACCTTCT
ACAAAAGTTGGATCTACTTAAAAATCTAGTTCTAATCCCTGCACCATTGGGAGGCATGA
ATTATA'TGAACATGAGCAGGTTATTGTTAGGAACATAGGTGACCCATTACTGCTTCAT
TTGCTGATATAAGCGCATGATCGAATGTGGGTATTAGGATGTAGCATTCTGTACAGA
TAATGTACCAAAAATGTGGITCCTCTAAATACCTAGACTGGCTAGTGATCCCTACTCAA
TAAACCTTCCTTATAGCCAAAGTATGACCAAGGTCTAAAAATGTAACAGCAAGATATG
TACTTATGCATAGCCCCAATCCTATGCTCAAAGATTGTTCCATGAAAAGTCACAAGAAG
AAGATGAAATCCTTGCTGAATTCTGTTAGACCGACACTAATAATCCCTAGAGCAC
ACGAAATTTATCAAATTCACTGACAGGTGCTAGGGAACTATAGCAGGTATGCTTGACA
CTACTAAGGGTTAACCGTGCTAGTATGTCAAGAGGTGGCTGACATCATCACTAGTT
TAAAATTATCAACATATGACTACCAACAGTTAGAACGTGTCTGAATGGCTTATGCTC
CTATCACGGGAATTGCTGTAAGCGTTGATTCTGTTCTGATTCTTAGCTAAGACCATCC
GAAAGAGAATGTGGGTCATCTAACTAACCGGAAGGGAGATTACGGGTTGGAGGTACCTG
ACATTITGGAATGCATGCAAAACAATATAATTATTGATCATGAAGATTGTTACTCATGTA
TTCAAGGATCAAAATATTATACATGGTTTTGTACCTCAAATTGTCAACTCGATCAGA
TAAATAAGTCACAAATTCTCCGAGTACCTTATGTTGGATCAACAACGTGAAGAAAGGA
GTGATATGAAGTTGTCATATGTGAGGTACCAAGTAGACCAACTAACGCAGTCGAA
TTGCACCGAGTATACATGGCTTATGGTGTGATGATTATCCTGGCATGAGGCTTGGT
ATTGGCAAGGACTAGGGCAAATATTACATTGATGAACCTAAATAACACCTATAG
CTACATCTACTAATTGGCACATAGGTTGAGAGATAGAACTCAAGTTAAATATTCA
GGACTTCCTTAGTAAGAGTGGCACGCTATACAACAATATCTAATGATAACATGTCCTCA
CTATTAACACAGGAAAGTCGATACTAATTGTTGATAGTACAGATGACTGATCAGCCTTACGC
TGAGTATACTCGAATACATATTCACTGATGACTGTACAAGTACTGGACAATCAAACACTGTA
TTCACCTACATGCAGATGTTAATTGTTGATAGTACAGATGACTGATCAGCCTTACGC
CAAGCTTAACTAAGAACGCTACCTGATATCAAACCCATCAATAATAATTGATATATGATC
CGGCTCCTATAATTGATACTGATGTCAGCTAGGTTGATTCTCAAAAATCTGTACATC
TAATAGATTTCCAAGTTGGTCAACTACTCAGCTAACACAGTGTGGCAAAAGTGGTAG
CACTATCTATAGTAGAATTGATCACAAAAGCGAGTAAAGACCATCTCAATGAGATAATAG

Figure 4-9

CGGTTGTTGGTATGATGATATCAATAGCTTATTACAGAATTCTACTTGTTGATCCAC
GTTTGTTCACACTATACTTAGGCCAACATACATGTCTTACAATGGGCATATGAAATCCATT
ATCATAGACCAGTGGCAGTACCAAGATGGCGAAGTATTACATAATTGCTGTCAAGAG
CTAGTAGAGGCATATTGACATATTGACCAATGCCTTAGCCATCCCCGGGTCTATAAAA
GATTCTGGGAATGTGGTTATTGGAGCCTATTATGGCCTATATAGGAAGTCAAAATC
TACATAGTGCAGTGATTATCTATAATGCATATCITACTTATTGGATGCTTATT
TATCTGATCAAGTAGATGATACTGATATTATAATCTGTGAAACAGAGGAGACATGTTAG
CAAATAGAATTGACAATTACCAAAGTAGACACCTAGCTGTACTCATAGACITGTACTGCG
ATTCCACTAGATGCCCAATATAAAAGGTCAGATAACAATTATGAGAAATTCAATCCTTA
GATCCTTCATTGATAATGAGAGGAAAACAAACCCACTCGGTTGACATGGAATCTGATC
CATTACTTGAGATCACTTAGCTGTTCTATTACATATCTAAGGAGAGGTATTATTAAC
AGATGAGATTAAGATTGACCCAAGCGTATCTCTGAATTATCTAGAATGATTAAACCTG
ATGTGATTATCAAGCACCTAAAGTCCGTCCTCATGGCTTATAGATATCAACCCCTG
AACTAAATGACCTTAATACAATTGGAGAGCTTAATAGCAAGTGGAAAGACATCCCTA
TAGGACAAATCAGAATCCAAAATTATGAAATACATGCATATAGGAGGATGGAGTTAATT
CAAATGCATGTTATAAGGCTTAGAGCTATTATCTGTTCTAAATCGGTTCATGTCTAAC
CATCAGGTGCATTGTTAGGTGAAGGGCAGGATCGATGCTGGTCACATATCGTGCCT
TTATTCCATTCAAGACAATTATATAATAGGTATTCAGTTCAAATGTTAGGGTC
AGAGAGAATTAAGTCTATATCCATCTGAAGTGGCACTAGTTGATAACAAAATCGCTTGG
CTAATGACCTTAATATCAAAGTCTGTTAATGGTAAGCCAGAGTCTACATGGTTGGAA
ATATTGACTGTTTGCTTATATTCTTAGCCATATTGAGACTTCAAGCTGACATTGATAC
ATAGTGATATTGAGTCCAGCTTGAGCAAGACAAAGAATAAAATTCTTGAGGAGCTGTGCC
ATATTCTGTCAATGGCACTCATTGGAAAGATCGGATCTTATTAGTTGTTAAGTTGC
TACCAAGGGTCAGTGATTACGTATTCTGAAATATGCATCAGAGTTCTATCAAC
AAAACCTTGTCTGCCTAGATTTAGTAACATGTCTCATCTGAGGTTACTACATAG
GAATTCACCTTAATACAAATCGATTGATTGACCTGATAGAATAGTACAATACATAATTA
GAAATTACAACCTACTCCAGTTACATTCTACATTGAAACTAAGTATCGAA
ATAATATGGTTACAAATTATGGACTATGCTTGTCAAGACGGACACAAAAGTGATTACTTGT

Figure 4-10

CATCAATTACAAAAATAGAGAGTGTCTCTGCATGTGGTTAGAATTGAACGGACCTA
AGATTATACAGCAATTATCAGGACATGACTATGCCAGTGGAGAGACTAGTCTGGAATCAA
GTATAATGATATTAGTTAGAGAATATCTTAATGCAACTATACAAGGCCGGAAACATTAG
GCTTGTTTCACCTTACCCGGTCCTCATGAGAGTCAGTTAACAGAGAAATCAATAAGTGA
TTGTATTGAAGTATATTGTATATCTGCTTTATTCAAACCTCTACATTATCTAGTAAAC
AAATAATGAGTAATCTTAGAAAAGGAATTGATGTATGATTGAGAGATGAGTTTCA
TATCAAGATTGTCAGCAAATTACAAGAAAAAGTAATGTCACAGGAAGTTAACAGTACCT
GGATATTAAATATTGATACTCCGACACGAAAGCGTTATATAAGTTAGTAGGTTACTCAT
TAATAATTAAATCACATATGAAGGTTGGCATGGTTATTCATTTTAAGGAGTAAGATAA
GACTTGATATATGATAACTGATTAAACATTACCTCTGAATTGAAGGATTGCTCAATTACA
TGGTTTTGAGTAATTGAGATTATTCCAATTAGTACAATTAGAAAAAACTTCAACAGT
TGATTGAGCCTTAATITACTCCACTAGCTATAITATAAGCTCGATAAAACTTGGT
TTGAAATTATAACAGTCATACCAATCTATCAAGGAAACACAATTGATGTCTAGTATGAAG
TTCATATTATATGTTTTAATCTTACCCACTCTAATTAGTCCTATTAAAGAATTAA
ATTATAGATGTTAACATGTTATATAATGGAAACCCTCAATGCTGCTATTGTTGGTAACCA
TAGGCATTGTATTAGATAATGTTATTCTTAGAAATGTGCAATCTCATACGTCGGACCC
CTCAGCCTCCCCCTTATAGTTCGTGATTGAAAAACACAAAAATAATCATGAATGGG
TGTACGTACCTATAGCTTCTTGCTGGT

Figure 5.

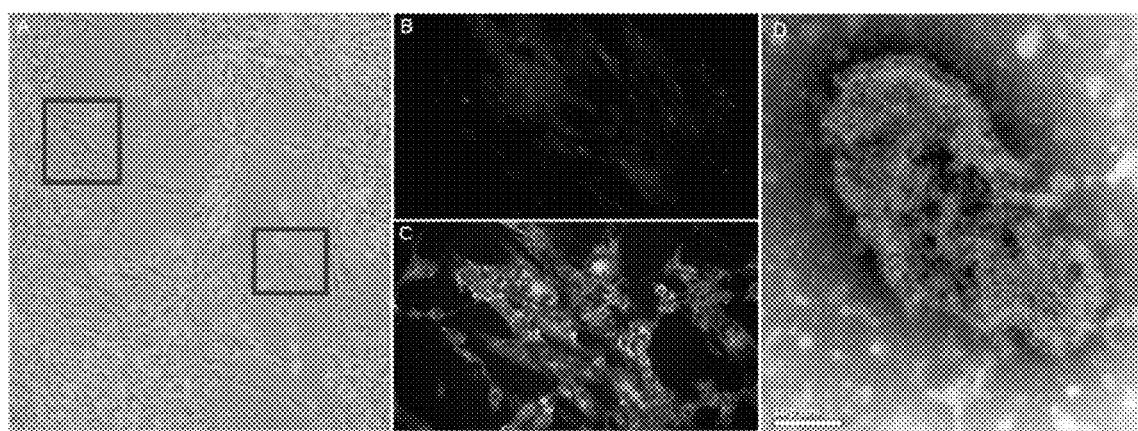
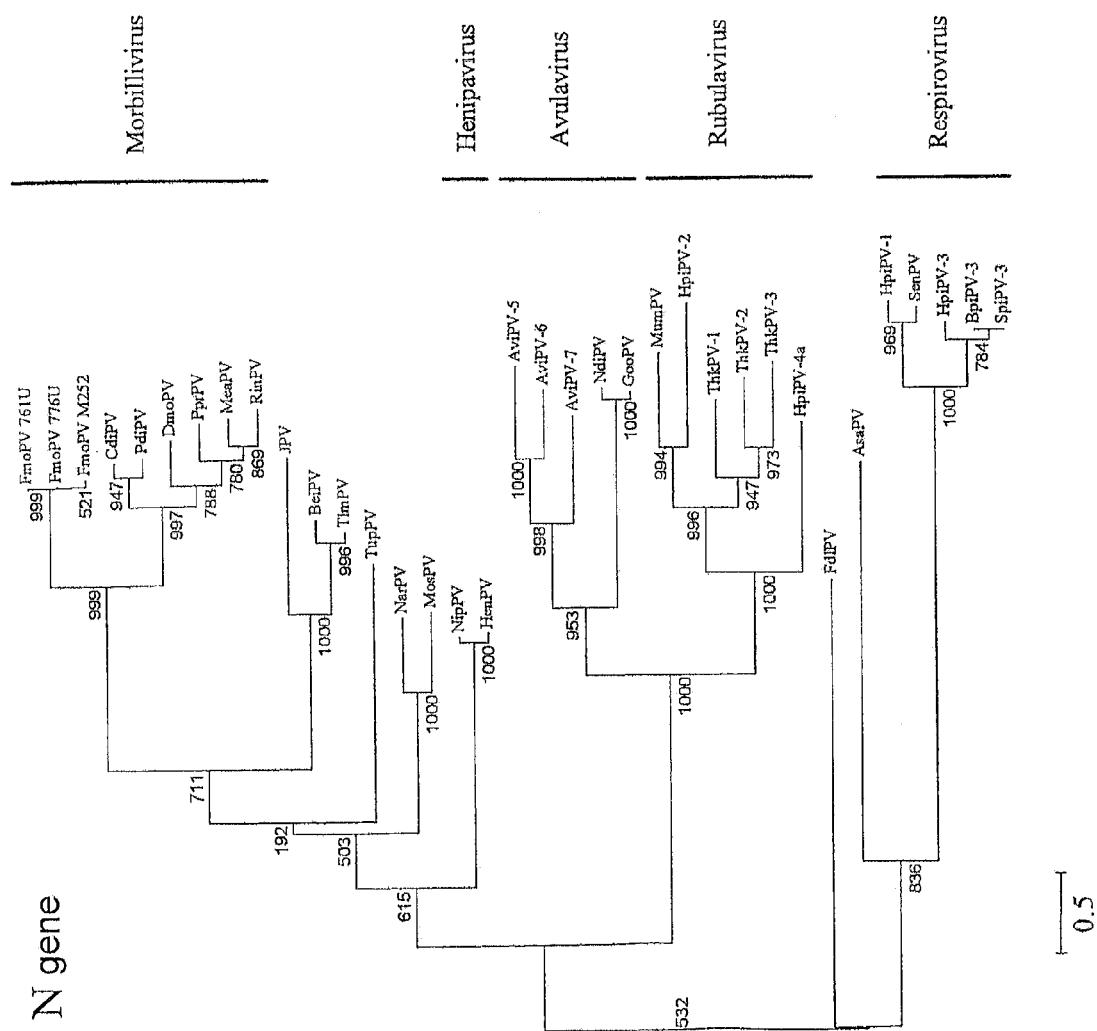
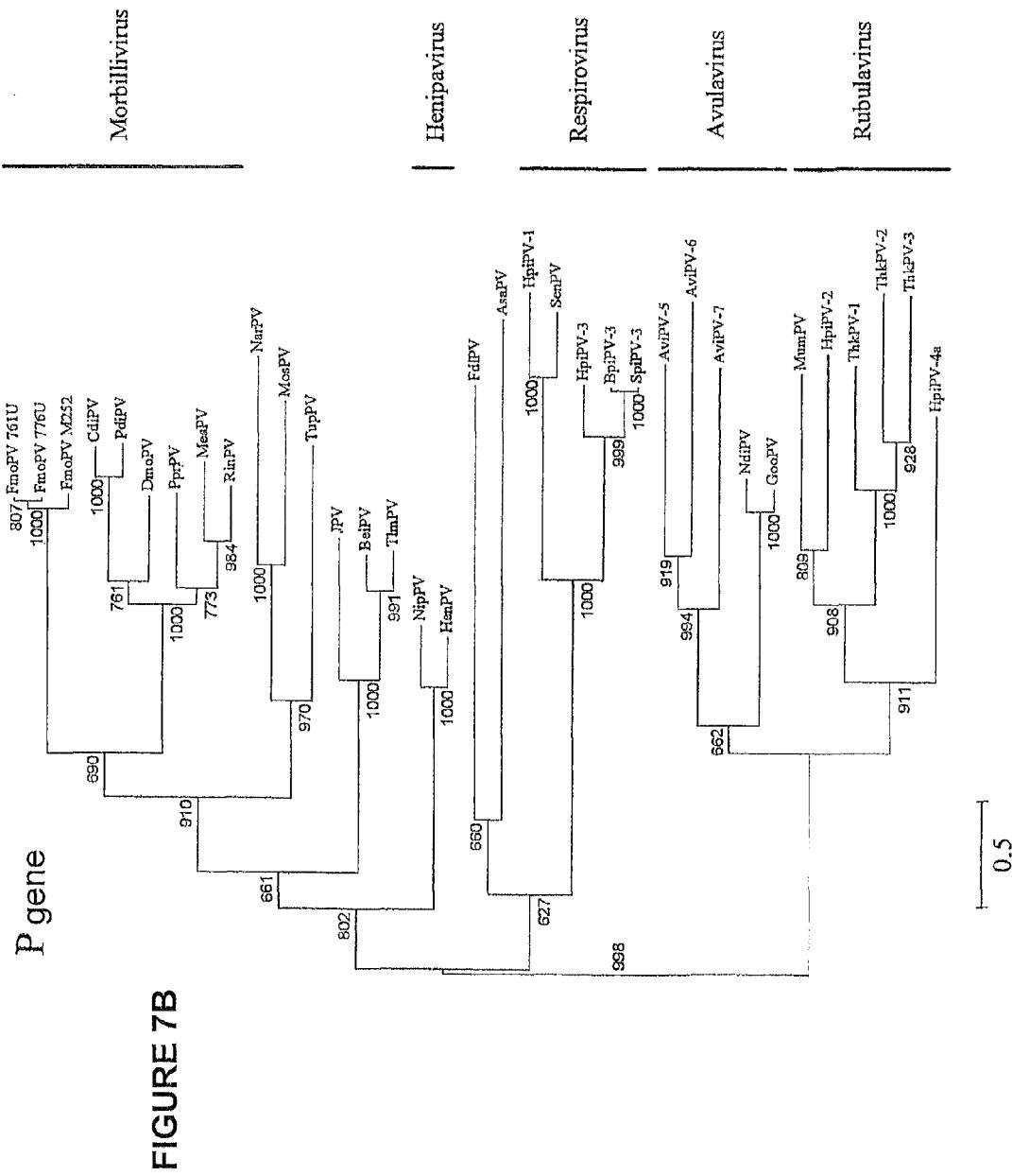
FIGURE 6

FIGURE 7A





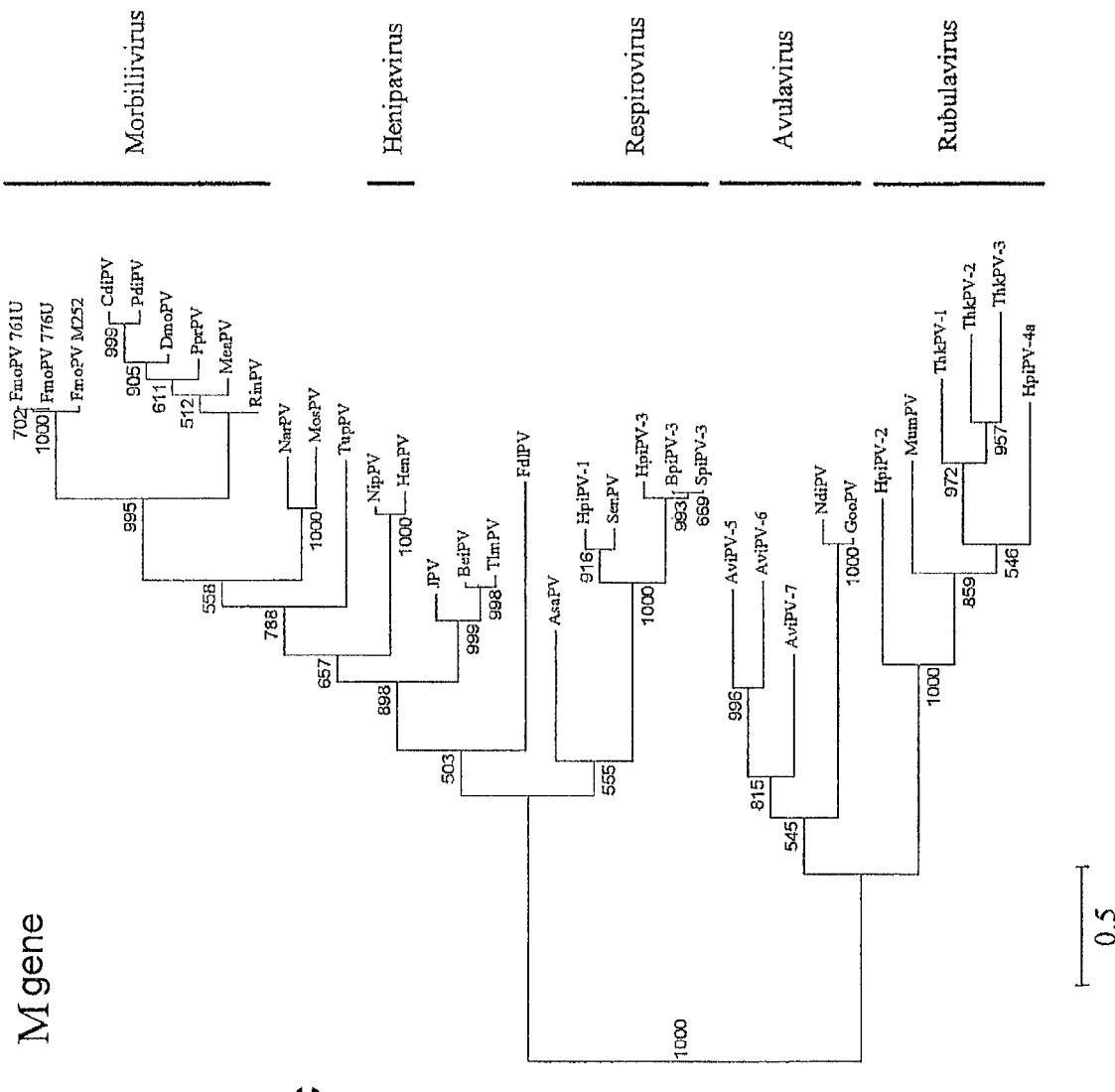
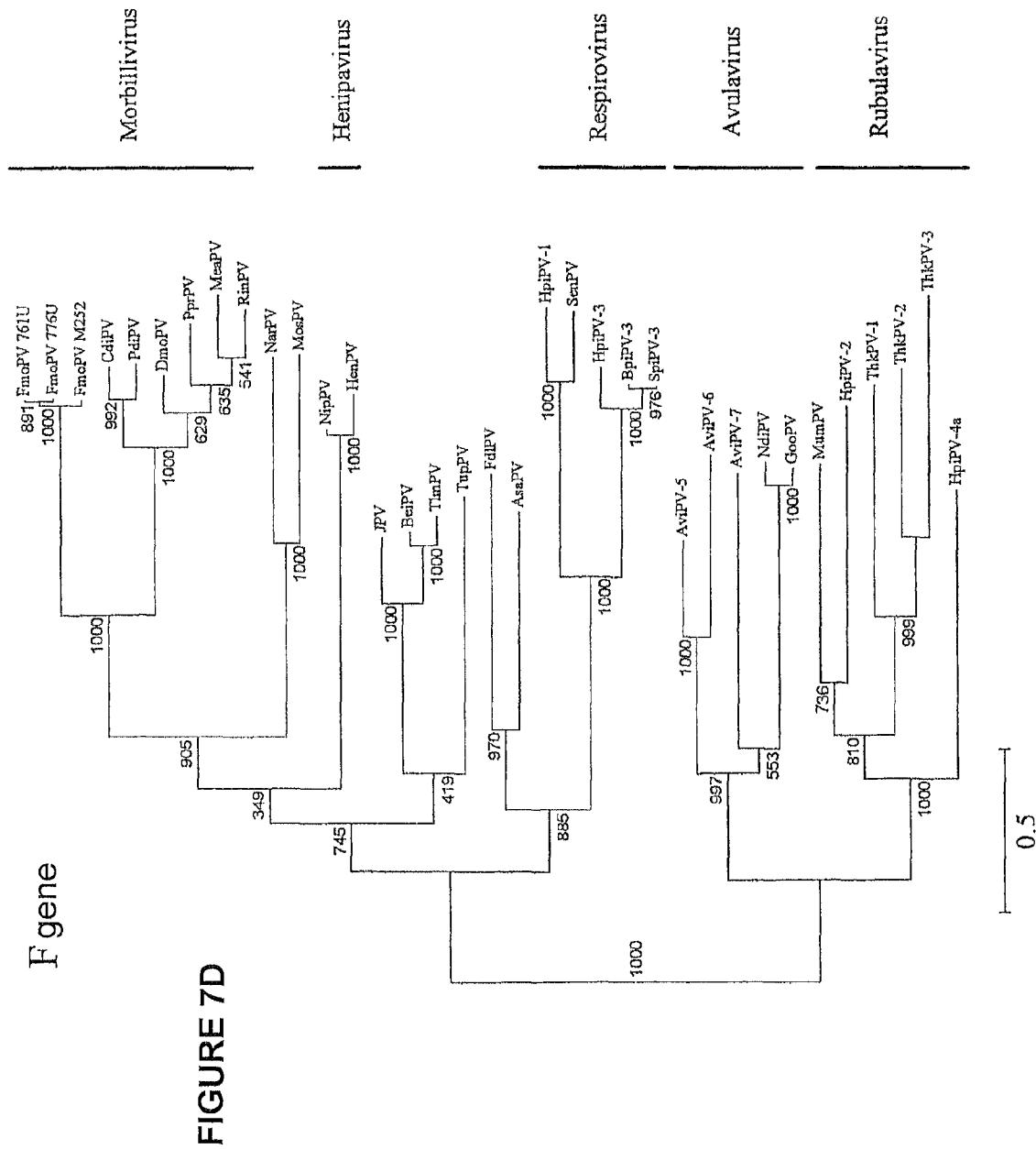
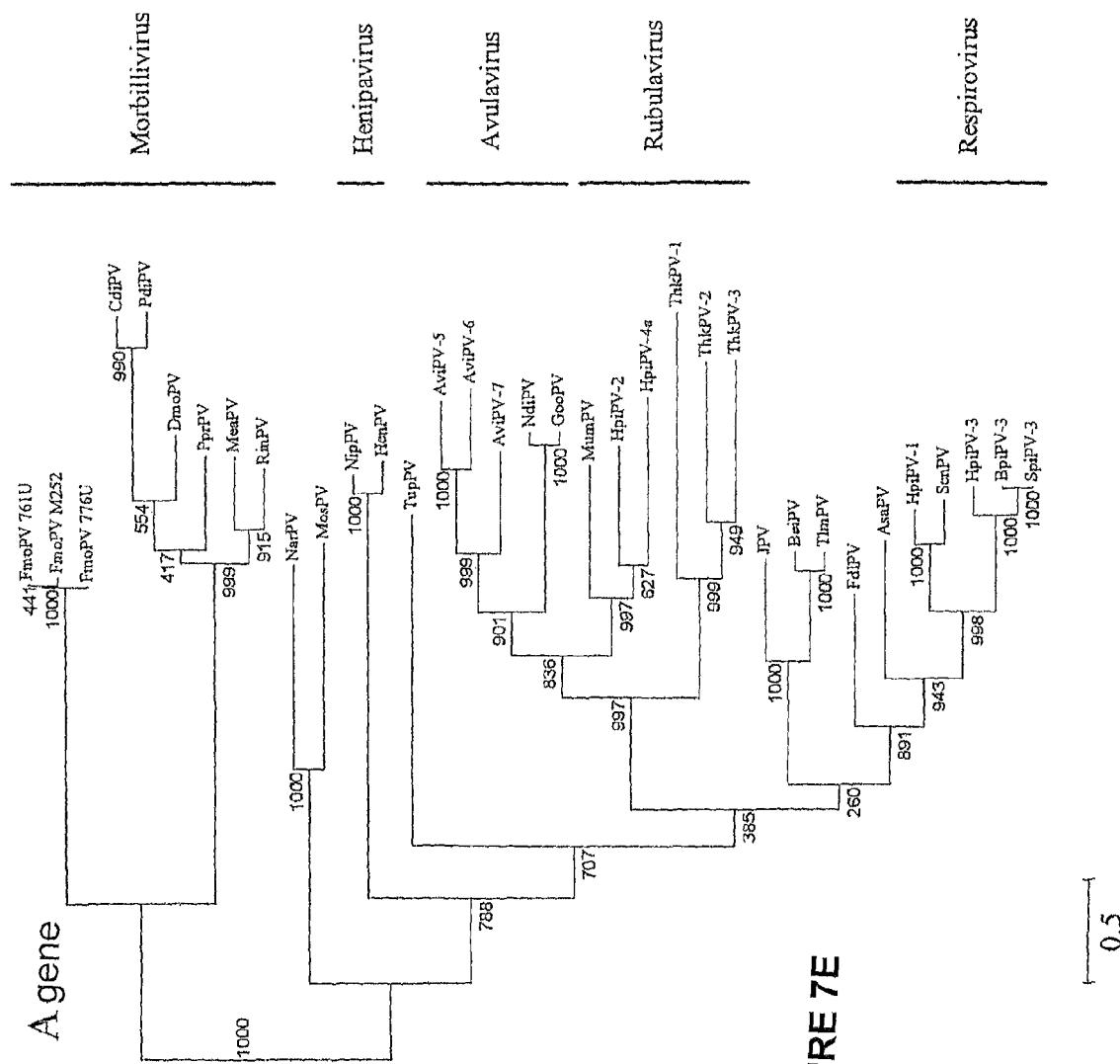


FIGURE 7C



**FIGURE 7E**

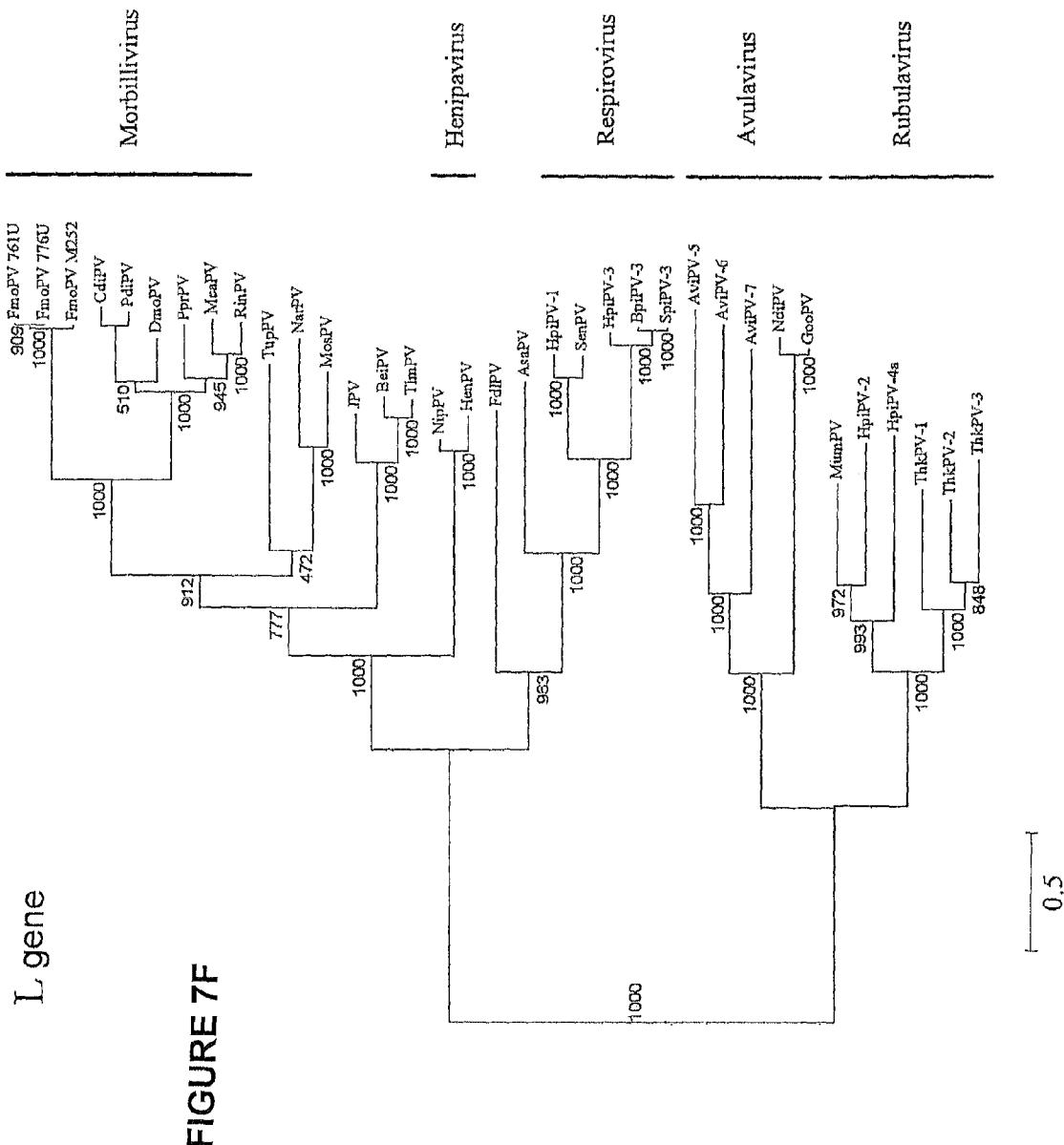


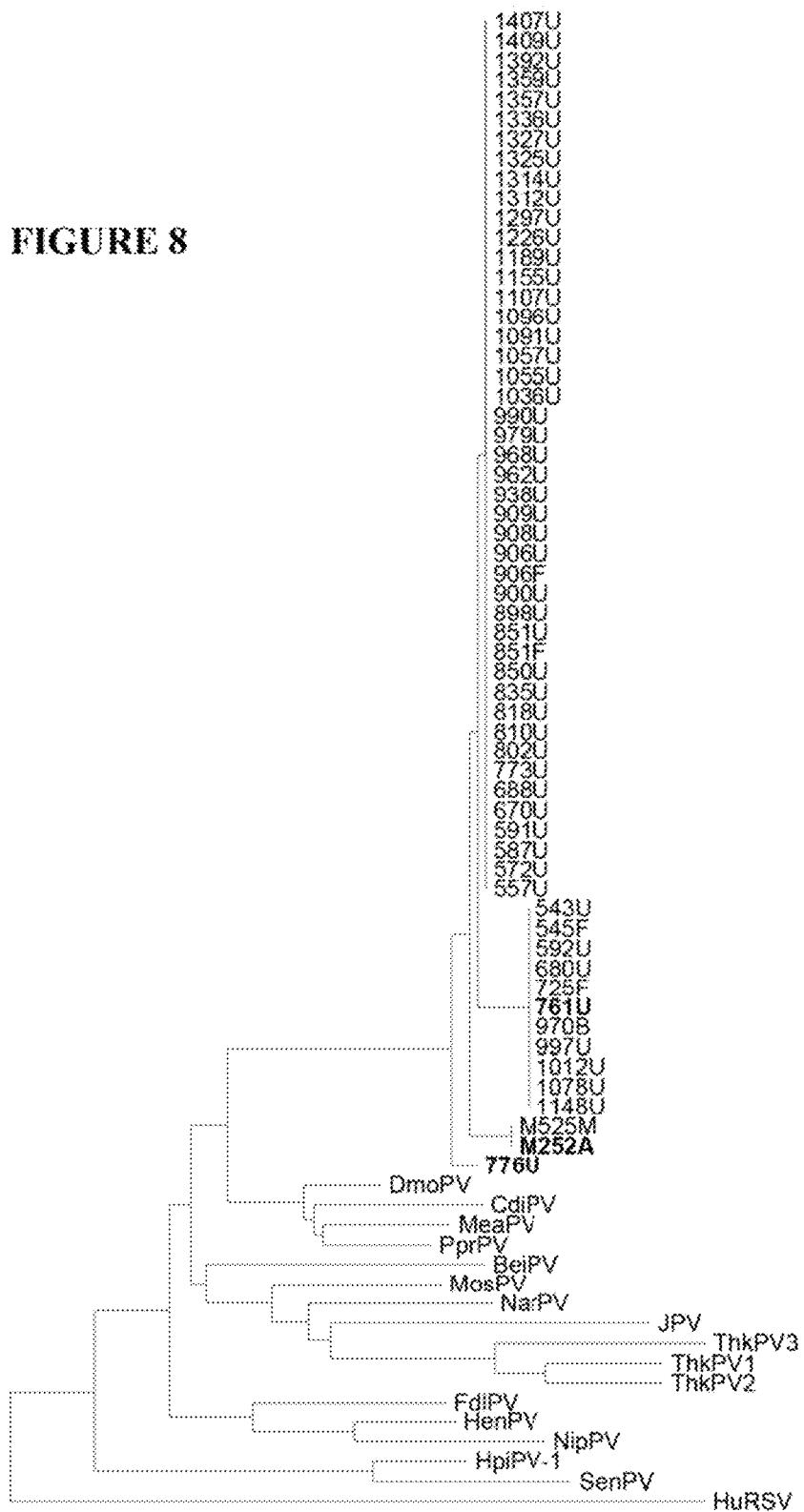
FIGURE 8

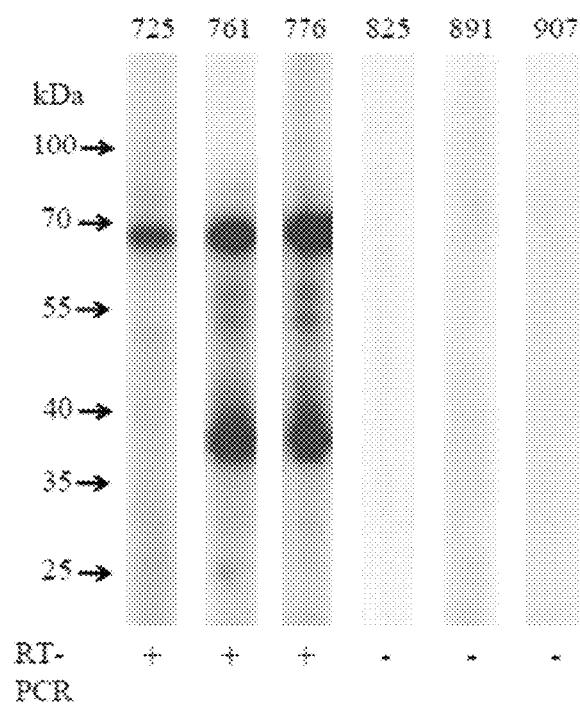
FIGURE 9

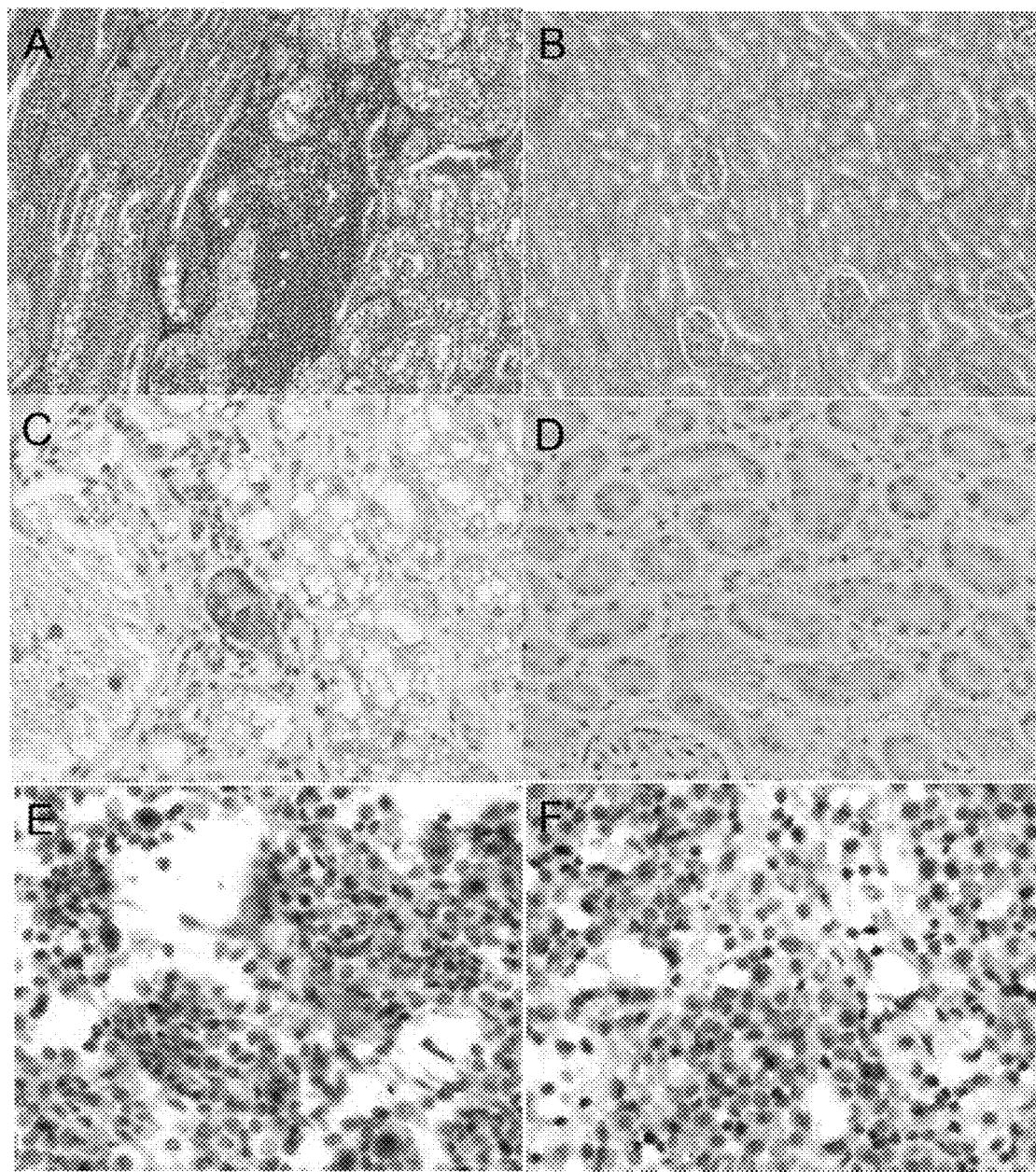
FIGURE 10

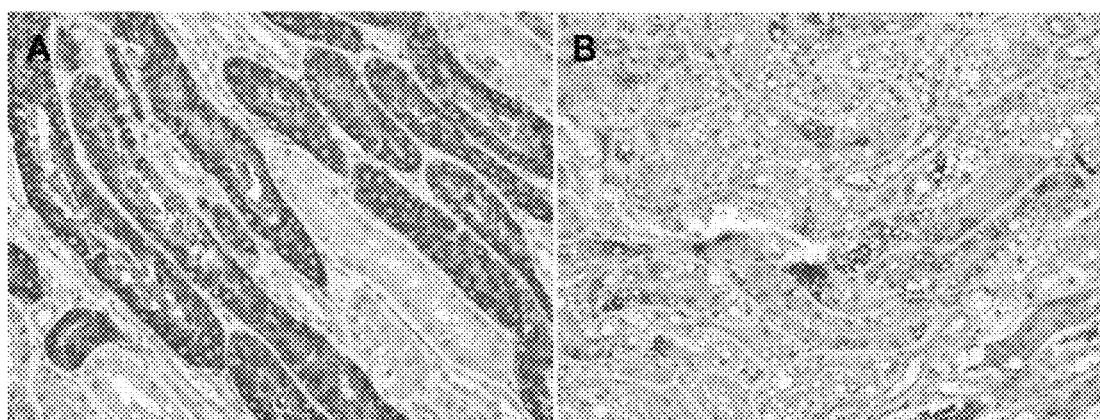
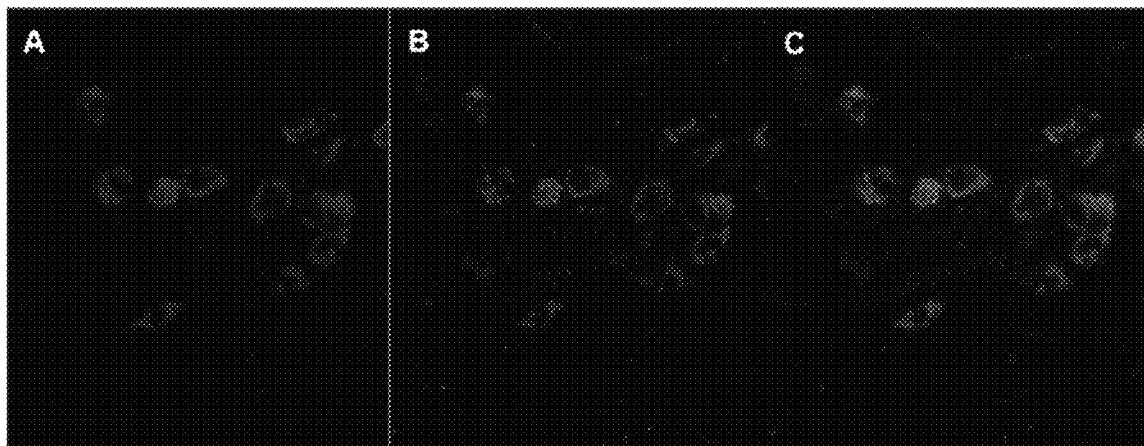
FIGURE 11

FIGURE 12

Mouse anti-Human
Myeloid/Histiocyte Antigen and
Texas-red conjugated Goat
anti-mouse IgG
(JacksonImmunoResearch,
West Grove, PA, USA)

Guinea Pig anti-NP and FITC
conjugated Rabbit anti-Guinea
pig IgG (Invitrogen, Camarillo •
CA, USA)

Merged image

FIGURE 13

>FmOPV 776U Cats/Hong Kong/2009_L
AGAGACTTAATGAGATTATGGACTGCCTGGATTTCCAGTGGCTTCACAAGATTTGGAGAAATCTGTTCTACGTTAGTG
ATCCATATAGTCCACCTGACTTTGATCAACATATCGATATAGAATCAGTCCAAACGACCATACTTTATCAAGTACCGATGG
GTGG
>FmOPV M252A Cats/China/2010_L
AGAGACTTAATGAAATTATGGATTGCCTGGGTTTTCACTGGCTTCACAAAATATTGGAGAAATCTGTTCTACGTTAGCG
ATCCGTCTAGTCCACCTGATTTGATCGACATATCGATATAGAATCAGTCCGAATGACCATACTTTATTAAGTACCGATGG
GTGG
>FmOPV 761U Cats/Hong Kong/2009_L
AGAGACTTAATGAAATTATGGACTGCCTGGATTTCCAGTGGCTTCACAAGATTTGGAGAAATCTGTTCTACGTTAGTG
ATCCATCTAGTCCACCTGACTTGATCAACATGTCATAGAATCAGTCCAAATGACCATACTTTATCAAGTACCGATGG
GTGG
>FmOPV 776U Cats/Hong Kong/2009_N protein
MSSLLRSLAAFKRHREQPTAPSGSGGTIKGLKNTIIVPVPGDTVITTRSNLLFRLVYIIGNPDPLSTST
GATISLLTLFVESPGQLIQRIADDPAVFKLVEVIEAGNPGELETFASRGINLDKQAQQYFKLAEKNNDQG
YYVSLGFENPPNDDITSSPEIFNYILASVLAQVVILLAKAVTAPDTAAEAENRRWIKLMQQRVDGELR
LSKGWLVLVRNKIASDITIRRFLVALVLDIKRSPGTRPRIAEMICDIDNYIVEAGLASFLLTIKFGIETR
YPALALHEFSGELATIEGLMKLYQSMGEMAPYMILENSIQTFRSAGSYPLLWSYAMGVGVEELERSMGL
NFTRSFDDPTYFRLGQEMVRSSGMVNSSFAREGLSEHETQLVSQIVNSGGESGIPKFDGFRANPTTFL
GTKDNINDRGEQDSNSISGLPGPPLLPSRDLNLSDSYGINSVGKVNVDKLNNEGVPDHDVSSSAMEELRR
LVESTNRIDTKQPEASGVTNHYNDTLLK
>FmOPV M252A Cats/China/2010_N protein
MSSLLRSLAAFKRHREQPTAPSGSGGTIKGLKNTIIVPVPGDTVITTRSNLLFRLVYIIGNPDPLSTST
GATISLLTLFVESPGQLIQRIADDPAVFKLVEVIEAGNPGELETFASRGINLDKQAQQYFKLAEKNNDQG
YYVSLGFENPPNDDITSSPEIFNYILASVLAQVVILLAKAVTAPDTAAEAENRRWIKLMQQRVDGELR
LSKGWLVLVRNKIASDITIRRFLVALVLDIKRSPGTRPRIAEMICDIDNYIVEAGLASFLLTIKFGIETR
YPALALHEFSGELATIEGLMKLYQSMGEMAPYMILENSIQTFRSAGSYPLLWSYAMGVGVEELERSMGL
NFTRSFDDPTYFRLGQEMVRSSGMVNSSFAREGLSEHETQLVSQIVNSGGESGIPKFDGFRANPTTFL
GTKDNINDRGEQDSNSISGLPGPPLLPSRDLNLSDSYGINSVGKVNVDKLNNEGVPDHDVSSSAMEELRR
LVESTNRIDTKKPEAPGVTNHYNDTLLR
>FmOPV 761U Cats/Hong Kong/2009_N protein
MSSLLRSLAAFKRHREQPTAPSGSGGAIKGLKNTIIVPVPGDTVITTRSNLLFRLVYIIGNPDPLSTST
GATISLLTLFVESPGQLIQRIADDPAVFKLVEVIEAGNPGELETFASRGINLDKQAQQYFKLAEKNNDQG
YYVSLGFENPPNDDITSSPEIFNYILASVLAQVVILLAKAVTAPDTAAEAENRRWIKLMQQRVDGELR
LSKGWLVLVRNKIASDITIRRFLVALVLDIKRSPGTRPRIAEMICDIDNYIVEAGLASFLLTIKFGIETR
YPALALHEFSGELATIEGLMKLYQSMGEMAPYMILENSIQTFRSAGSYPLLWSYAMGVGVEELERSMGL
NFTRSFDDPTYFRLGQEMVRSSGMVNSSFAREGLSDHETQLVSQIVNSGGESGIPKFDGFRANPTTFL
GTKDNINDRGEQDSNSISGLPGPPLLPSRDLNLSDSYGINSVGKVNVDKLNNEGVPDHDVSSSAMEELRR
LVESTNRIDTKQPEASGVTNHYNDTLLK

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**FELINE MORBILLIVIRUS AND USES
THEREOF**

**CROSS-REFERENCE TO RELATED
APPLICATIONS**

The present application claims the benefit of U.S. patent application Ser. No. 61/588,778, filed Jan. 20, 2012, which is hereby incorporated by reference in its entirety.

SEQUENCE LISTING

The instant application contains a Sequence Listing which has been submitted in ASCII format via EFS-Web and is hereby incorporated by reference in its entirety. Said ASCII copy, created on Apr. 30, 2013, is named Sequence_Listing_2748US1.txt and is 108,282 bytes in size.

INTRODUCTION

Described herein are isolated *paramyxovirus*, a *morbillovirus* (FmoPV), isolated nucleic acids encoding the genome of FmoPV, isolated amino acid sequences of FmoPV proteins, antibodies to FmoPV and its proteins, and uses thereof. In certain embodiments, the modified FmoPV is a feline *morbillovirus*. Also described herein is a recombinant FmoPV comprising a modified FmoPV gene or gene segments and the use of such a virus. The recombinant FmoPV may be used in the prevention and/or treatment of diseases related to FmoPV or as a delivery vector. Also described herein is a diagnostic assay for the FmoPV. In certain embodiments, the FmoPV causes kidney disease. In certain embodiments, the kidney disease is in felines. In certain embodiments, the kidney disease is tubulointerstitial nephritis ("TIN"). Also described herein is a quantitative assay for the detection of the FmoPV, natural or artificial variants, analogs, or derivatives thereof. In certain embodiments, the quantitative assay is reverse transcription and polymerase chain reaction (RT-PCR). Also described herein is a vaccine and a kit containing the vaccine for the prevention and treatment of FmoPV infection. Described herein is a diagnostic kit that comprises nucleic acid molecules for the detection of the FmoPV.

1. BACKGROUND OF THE INVENTION

Paramyxoviruses are enveloped, negative-sense single-stranded RNA viruses that are divided into two subfamilies, Paramyxovirinae and Pneumovirinae. Viruses in the subfamily Paramyxovirinae have been associated with a number of emerging diseases in humans and various animals in the past two decades (1-9). There are currently five genera within the subfamily Paramyxovirinae, namely *Respirovirus*, *Rubulavirus*, *Morbillivirus*, *Henipavirus* and *Avulavirus*, although some members of the subfamily remain unclassified. Among members of Paramyxovirinae, measles virus, mumps virus, and human parainfluenza viruses 1 to 4 are most well known human *paramyxoviruses* which cause outbreaks of respiratory to systemic infections (10-12). Three novel *rubulaviruses*, *Tuhoko* virus 1, 2 and 3, from fruit bats in mainland China and a novel unclassified *paramyxovirus*, *Tailam* virus, from Sikkim rats in Hong Kong were recently reported (13, 14). Despite the presence of *paramyxoviruses* in a variety of animals, no *paramyxoviruses* have been naturally observed in cats, although there is controversial evidence that cats may be infected with parainfluenza 5 virus (15,16).

Cats and dogs are the most common domestic animals and pets worldwide. As a result of their close relatedness, inter-

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species jumping of viruses among these two kinds of animals is not uncommon. For *coronaviruses*, feline *coronavirus* and canine *coronavirus* are classified under the same species *Alphacoronavirus* 1, and feline *coronavirus* type II strains were generated by double homologous recombination between feline *coronavirus* type I strains and canine *coronavirus* (17). For *parvoviruses*, the fatal canine *parvovirus* that emerged in the 1970s also originated from a feline *parvovirus*, feline panleukopenia virus (18,19). As for herpesviruses, canid herpesvirus 1 and felid herpesvirus 1 are closely related and are classified under the genus *Varicellovirus* (20). Furthermore, for papillomaviruses, canine oral papillomavirus and feline papillomavirus are also closely related and are classified under the genus *Lambdapapillomavirus* (21). Dogs are well-known hosts of a *paramyxovirus*, canine distemper virus, in the genus *Morbillovirus* (22), but no *paramyxoviruses* have ever been discovered in domestic cats.

Many feline diseases have no known causes. For example, the cause of most cases of feline tubulointerstitial nephritis is hitherto unknown and therefore treatment is mainly supportive and prevention is difficult. Tubulointerstitial nephritis ("TIN") involves primary injury to renal tubules and interstitium and is the most common cause of renal failure and one of the leading causes of deaths in cats. However, the cause of most cases of feline TIN remains unknown and therefore treatment is mainly supportive and prevention is difficult. With millions of cats in households around the world, the disease burden from TIN is great. For example, in the United States of America, it is estimated that there are 75 million household cats, while there are an estimated 8 million household cats in United Kingdom (data from Chomel B B, Sun B., Zoo noses in the bedroom. Emerg Infect Dis. 2011 February; 17(2):167-72.). The capability to diagnose, treat or prevent feline kidney or other diseases would have a great benefit.

The citation of any reference herein should not be construed as an admission that such reference is available as "prior art" to the instant application.

2. SUMMARY OF THE INVENTION

In one aspect, provided herein are nucleic acid sequences comprising or consisting of a wild-type or a modified FmoPV gene segment (genomic RNA) or the complement thereof (antigenomic RNA). Also described herein are isolated nucleic acids encoding the genome of FmoPV, polypeptides encoded by portions of the isolated FmoPV, nucleic acids, primers, vectors, host cells, antibodies to FmoPV and to FmoPV polypeptides, immunogenic compositions, diagnostic methods, screening assays, methods of treatment and related uses.

In one aspect, described herein is a novel *paramyxovirus* in the genus *Morbillovirus*, a feline *morbillovirus* (hereinafter "FmoPV") from domestic cat (*Felis catus*). Also described herein is that this novel FmoPV virus is associated with tubulointerstitial nephritis (TIN) in cats.

In one aspect, the modified FmoPV gene segment comprises FmoPV nucleic acid sequence and also a heterologous nucleotide sequence. In some embodiments, the first and second heterologous nucleotide sequences encode different peptides or polypeptides. In other embodiments, the first and second heterologous nucleotide sequences encode the same peptide or polypeptides. In specific embodiments, a FmoPV comprising a modified FmoPV gene segment described herein achieves titers of approximately 3×10^5 pfu/ml, 3.5×10^5 pfu/ml, 4×10^5 pfu/ml, 5×10^5 pfu/ml, 1×10^6 pfu/ml, 5×10^6 pfu/ml, 1×10^7 pfu/ml, 5×10^7 pfu/ml, 1×10^8 pfu/ml, 5×10^8 pfu/ml, 1×10^9 pfu/ml or more after 1, 2, 3, 4, 5, 6, 7, 8, 9, 10

or more passages in cells (e.g., MDCK cells) or embryonated chick eggs. In certain embodiments, a FmoPV described herein comprises an attenuating mutation. In one aspect, provided herein are methods of using a FmoPV, wherein the FmoPV comprises a modified FmoPV gene segment.

In one embodiment, provided herein are methods for detecting the presence or expression of FmoPV, natural or artificial variants, analogs, or derivatives thereof, in a biological material, such as cells, blood, serum, plasma, saliva, urine, stool, sputum, nasopharyngeal aspirates, and so forth. The increased or decreased activity or expression of FmoPV in a sample relative to a control sample can be determined by contacting the biological material with an agent which can detect directly or indirectly the presence or expression of FmoPV. In a specific embodiment, the detecting agents are nucleic acid molecules of the present invention.

In a specific embodiment, provided herein is a diagnostic assay for FmoPV, natural or artificial variants, analogs, or derivatives thereof. In particular, provided herein is a quantitative assay for the detection of nucleic acid molecules of FmoPV using reverse transcription and polymerase chain reaction (RT-PCR). Also provided in the present invention are nucleic acid molecules that are suitable for hybridization to FmoPV nucleic acids such as, including, but not limited to, PCR primers, Reverse Transcriptase primers, probes for Southern analysis or other nucleic acid hybridization analysis for the detection of FmoPV nucleic acids. Said FmoPV nucleic acids consist of or comprise the nucleic acid sequence as described infra or a complement, analog, derivative, or fragment thereof, or a portion thereof.

In one aspect, the invention relates to the use of the isolated FmoPV for diagnostic methods. In a specific embodiment, the invention provides a method of detecting mRNA or genomic RNA of FmoPV of the invention in a biological material, such as cells, blood, serum, plasma, saliva, urine, stool, sputum, nasopharyngeal aspirates, and so forth. The increased or decreased level of mRNA or genomic RNA of FmoPV in a sample relative to a control sample can be determined by contacting the biological material with an agent which can detect directly or indirectly the mRNA or genomic RNA of FmoPV. In a specific embodiment, the detecting agents are the nucleic acid molecules of the present invention.

The present invention also relates to a method of identifying a subject infected with FmoPV, natural or artificial variants, analogs, or derivatives thereof. In a specific embodiment, the method comprises obtaining total RNA from a biological sample obtained from the subject; reverse transcribing the total RNA to obtain cDNA; and subjecting the cDNA to PCR assay using a set of primers derived from a nucleotide sequence of FmoPV.

The present invention further relates to a diagnostic kit comprising primers and a nucleic acid probe for the detection of mRNA or genomic RNA of FmoPV. In a specific embodiment, provided herein is a diagnostic kit comprising nucleic acid molecules which are suitable for use to detect FmoPV, natural or artificial variants, analogs, or derivatives thereof. In one embodiment, a kit provided herein comprises, in one or more containers, a nucleic acid sequence described herein. In another embodiment, a kit provided herein, comprises, in one or more containers, a FmoPV described herein.

In another aspect, provided herein are substrates (e.g., host cells and eggs) comprising a nucleic acid sequence described herein.

In one embodiment, provided herein is a method for eliciting an immune response against FmoPV in a subject, wherein the method comprises administering a FmoPV described herein or a composition thereof to the subject. In

another embodiment, provided herein is a method of preventing and/treating FmoPV infection in a subject, wherein the method comprises administering a FmoPV described herein or a composition thereof to the subject. In another embodiment, provided herein is a method for preventing and/or treating an FmoPV disease in a subject, wherein the method comprises administering a FmoPV described herein or a composition thereof to the subject.

In another embodiment, provided herein are methods for eliciting an immune response against an antigen in a subject, comprising administering a FmoPV described herein or a composition thereof to the subject. In another embodiment, provided herein are methods for generating or identifying antibodies that bind to a FmoPV utilizing a FmoPV described herein or a composition thereof.

In another aspect, the FmoPV described herein can be used to assess the antiviral activity of a compound or understand the life cycle of a FmoPV.

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2.1 Terminology

As used herein, the term "variant" refers either to a naturally occurring genetic mutant of the FmoPV or a recombinantly prepared variation of the FmoPV, each of which contain one or more mutations in its genome compared to the FmoPV having a nucleic acid sequence disclosed in Genbank accession nos. JQ411014, JQ411015 and JQ411016. The term "variant" may also refer to either a naturally occurring variation of a given peptide or a recombinantly prepared variation of a given peptide or protein in which one or more amino acid residues have been modified by amino acid substitution, addition, or deletion.

As used herein, the term "mutant" refers to the presence of mutations in the nucleotide sequence of an organism as compared to a wild-type organism.

As used herein, the terms "antibody" and "antibodies" refer to monoclonal antibodies, bispecific antibodies, multi-specific antibodies, human antibodies, humanized antibodies, chimeric antibodies, camelised antibodies, single domain antibodies, single-chain Fvs (scFv), single chain antibodies, Fab fragments, F(ab') fragments, disulfide-linked Fvs (sdFv), and anti-idiotypic (anti-Id) antibodies (including, e.g., anti-Id antibodies to antibodies of the invention), and epitope-binding fragments of any of the above. In particular, antibodies include immunoglobulin molecules and immunologically active fragments of immunoglobulin molecules, i.e., molecules that contain an antigen binding site. Immunoglobulin molecules can be of any type (e.g., IgG, IgE, IgM, IgD, IgA and IgY), class (e.g., IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2), or subclass.

As used herein, the term "antibody fragment" refers to a fragment of an antibody that immunospecifically binds to a FmoPV or any epitope of the FmoPV. Antibody fragments may be generated by any technique known to one of skill in the art. For example, Fab and F(ab')₂ fragments may be produced by proteolytic cleavage of immunoglobulin molecules, using enzymes such as papain (to produce Fab fragments) or pepsin (to produce F(ab')₂ fragments). F(ab')₂ fragments contain the complete light chain, and the variable region, the CH1 region and the hinge region of the heavy chain. Antibody fragments can be also produced by recombinant DNA technologies. Antibody fragments may be one or more complementarity determining regions (CDRs) of antibodies.

As used herein, the term "an antibody or an antibody fragment that immunospecifically binds a polypeptide of the invention" refers to an antibody or a fragment thereof that immunospecifically binds to the polypeptide encoded by the

nucleic acid sequence of the FmoPV, or a complement, analog, derivative, or fragment thereof, or a portion thereof, or that immunospecifically binds to the polypeptide of the FmoPV, or a variant, analog, derivative, or fragment thereof, and does not non-specifically bind to other polypeptides. An antibody or a fragment thereof that immunospecifically binds to the polypeptide of the invention may cross-react with other antigens. Preferably, an antibody or a fragment thereof that immunospecifically binds to a polypeptide of the invention does not cross-react with other antigens. An antibody or a fragment thereof that immunospecifically binds to the polypeptide of the invention, can be identified by, for example, immunoassays or other techniques known to those skilled in the art.

As used herein, the term "epitope" refers to a fragment of FmoPV peptide, polypeptide or protein having antigenic or immunogenic activity in an animal, preferably a mammal, and most preferably in a feline. An epitope having immunogenic activity is a fragment of a polypeptide that elicits an antibody response in an animal. An epitope having antigenic activity is a fragment of a polypeptide or protein to which an antibody immunospecifically binds as determined by any method well known in the art, for example, by the immunoassays described herein. Antigenic epitopes need not necessarily be immunogenic.

As used herein, the term "antigenicity" refers to the ability of a substance (e.g., foreign objects, microorganisms, drugs, antigens, proteins, peptides, polypeptides, nucleic acids, DNA, RNA, etc.) to trigger an immune response in a particular organism, tissue, and/or cell. Sometimes, the term "antigenic" is synonymous with the term "immunogenic".

As used herein, the term "immunogenicity" refers to the property of a substance (e.g., foreign objects, microorganisms, drugs, antigens, proteins, peptides, polypeptides, nucleic acids, DNA, RNA, etc.) being able to evoke an immune response within an organism. Immunogenicity depends partly upon the size of the substance in question and partly upon how unlike the host molecules is the substance. Highly conserved proteins tend to have rather low immunogenicity.

As used herein, the term "hybridizes under stringent conditions" describes conditions for hybridization and washing under which nucleotide sequences having at least 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95% identity to each other typically remain hybridized to each other. Such hybridization conditions are described in, for example but not limited to, Current Protocols in Molecular Biology, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6.; Basic Methods in Molecular Biology, Elsevier Science Publishing Co., Inc., N.Y. (1986), pp. 75-78, and 84-87; and Molecular Cloning, Cold Spring Harbor Laboratory, N.Y. (1982), pp. 387-389, and are well known to those skilled in the art. A preferred, non-limiting example of stringent hybridization conditions is hybridization in 6× sodium chloride/sodium citrate (SSC), 0.5% SDS at about 68° C. followed by one or more washes in 2×SSC, 0.5% SDS at room temperature. Another preferred, non-limiting example of stringent hybridization conditions is hybridization in 6×SSC at about 45° C. followed by one or more washes in 0.2×SSC, 0.1% SDS at about 50° C. to 65° C.

An "isolated" or "purified" peptide or protein is substantially free of cellular material or other contaminating proteins from the cell or tissue source from which the protein is derived, or is substantially free of chemical precursors or other chemicals when chemically synthesized. The language "substantially free of cellular material" includes preparations of a polypeptide/protein in which the polypeptide/protein is

separated from cellular components of the cells from which it is isolated or recombinantly produced. Thus, a polypeptide/protein that is substantially free of cellular material includes preparations of the polypeptide/protein having less than about 30%, 20%, 10%, 5%, 2.5%, or 1%, (by dry weight) of contaminating protein. When the polypeptide/protein is recombinantly produced, it is also preferably substantially free of culture medium, i.e., culture medium represents less than about 20%, 10%, or 5% of the volume of the protein preparation. When polypeptide/protein is produced by chemical synthesis, it is preferably substantially free of chemical precursors or other chemicals, i.e., it is separated from chemical precursors or other chemicals which are involved in the synthesis of the protein. Accordingly, such preparations of the polypeptide/protein have less than about 30%, 20%, 10%, 5% (by dry weight) of chemical precursors or compounds other than the polypeptide/protein fragment of interest. In a preferred embodiment, the polypeptides/proteins are isolated or purified.

As used herein, the term "isolated" virus is one which is separated from other organisms which are present in the natural source of the virus, e.g., biological material such as cells, blood, serum, plasma, saliva, urine, stool, sputum, nasopharyngeal aspirates, and so forth. The isolated virus can be used to infect a subject.

As used herein, the term "having a biological activity of the polypeptides of the invention" refers to the characteristics of the polypeptides or proteins having a common biological activity similar or identical structural domain and/or having sufficient amino acid identity to the polypeptide encoded by the nucleotide sequence of FmoPV or a complement, analog, derivative, or fragment thereof, or a portion thereof, or the polypeptide having the amino acid sequence of FmoPV, or a variant, analog, derivative, or fragment thereof. Such common biological activities of the polypeptides of the invention include antigenicity and immunogenicity.

As used herein, the term "portion" or "fragment" refers to a fragment of a nucleic acid molecule containing at least about 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100, 150, 200, 250, 300, 350, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950, 1000, 1050, 1100, 1150, 1200, 2,000, 3,000, 4,000, 5,000, 6,000, 7,000, 8,000, 9,000, 10,000, 11,000, 12,000, 13,000, 14,000, 15,000, 16,000, 17,000 or more contiguous nucleic acids in length of the relevant nucleic acid molecule and having at least one functional feature of the nucleic acid molecule (or the encoded protein has one functional feature of the protein encoded by the nucleic acid molecule); or a fragment of a protein or a polypeptide containing at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 90, 100, 120, 140, 160, 180, 200, 220, 240, 260, 280, 300, 320, 340, 360, 380, 400, 500, 600, 800, 1,000, 2,000, 3,000, 4,000, 5,000, 6,000, 7,000, 8,000, 9,000, 9,500 or more amino acid residues in length of the relevant protein or polypeptide and having at least one functional feature of the protein or polypeptide.

As used herein, the term "analogue" (e.g., proteins, polypeptides, peptides, and antibodies) refers to an agent that possesses a similar or identical function as a second agent but does not necessarily comprise a similar or identical amino acid sequence of the second agent, or possess a similar or identical structure of the second proteinaceous agent. In a specific embodiment, antibody analogues immunospecifically bind to the same epitope as the original antibodies from which the analogues were derived. In an alternative embodiment, antibody analogues immunospecifically bind to different epitopes than the original antibodies from which the analogues were derived. An agent that has a similar amino acid

sequence refers to a second agent that satisfies at least one of the following: (a) an agent having an amino acid sequence that is at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95% or at least 99% identical to the amino acid sequence of a second agent; (b) an agent encoded by a nucleotide sequence that hybridizes under stringent conditions to a nucleotide sequence encoding a second agent of at least 5 contiguous amino acid residues, at least 10 contiguous amino acid residues, at least 15 contiguous amino acid residues, at least 20 contiguous amino acid residues, at least 25 contiguous amino acid residues, at least 40 contiguous amino acid residues, at least 50 contiguous amino acid residues, at least 60 contiguous amino residues, at least 70 contiguous amino acid residues, at least 80 contiguous amino acid residues, at least 90 contiguous amino acid residues, at least 100 contiguous amino acid residues, at least 125 contiguous amino acid residues, or at least 150 contiguous amino acid residues; and (c) an agent encoded by a nucleotide sequence that is at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95% or at least 99% identical to the nucleotide sequence encoding a second agent. An agent with similar structure to a second agent refers to an agent that has a similar secondary, tertiary or, quaternary structure to the second agent. The structure of an agent can be determined by methods known to those skilled in the art, including but not limited to, peptide sequencing, X ray crystallography, nuclear magnetic resonance, circular dichroism, and crystallographic electron microscopy.

To determine the percent identity of two amino acid sequences or of two nucleic acid sequences, the sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in the sequence of a first amino acid or nucleic acid sequence for optimal alignment with a second amino acid or nucleic acid sequence). The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position. The percent identity between the two sequences is a function of the number of identical positions shared by the sequences (i.e., % identity=number of identical overlapping positions/total number of positions×100%). In one embodiment, the two sequences are the same length.

The determination of percent identity between two sequences can also be accomplished using a mathematical algorithm. A preferred, non limiting example of a mathematical algorithm utilized for the comparison of two sequences is the algorithm of Karlin and Altshul, 1990, Proc. Natl. Acad. Sci. U.S.A. 87:2264 2268, modified as in Karlin and Altshul, 1993, Proc. Natl. Acad. Sci. U.S.A. 90:5873 5877. Such an algorithm is incorporated into the NBLAST and XBLAST programs of Altschul et al., 1990, J. Mol. Biol. 215:403. BLAST nucleotide searches can be performed with the NBLAST nucleotide program parameters set, e.g., for score=100, wordlength=12 to obtain nucleotide sequences homologous to a nucleic acid molecules of the present invention. BLAST protein searches can be performed with the XBLAST program parameters set, e.g., to score 50, wordlength=3 to obtain amino acid sequences homologous to a protein molecule of the present invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al., 1997, Nucleic Acids

Res. 25:3389 3402. Alternatively, PSI BLAST can be used to perform an iterated search which detects distant relationships between molecules (Id.). When utilizing BLAST, Gapped BLAST, and PSI Blast programs, the default parameters of the respective programs (e.g., of XBLAST and NBLAST) can be used (see, e.g., the NCBI website). Another preferred, non limiting example of a mathematical algorithm utilized for the comparison of sequences is the algorithm of Myers and Miller, 1988, CABIOS 4:11 17. Such an algorithm is incorporated in the ALIGN program (version 2.0) which is part of the GCG sequence alignment software package. When utilizing the ALIGN program for comparing amino acid sequences, a PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 can be used.

The percent identity between two sequences can be determined using techniques similar to those described above, with or without allowing gaps. In calculating percent identity, typically only exact matches are counted.

As used herein, the term "derivative" (e.g., proteins, polypeptides, peptides, and antibodies) refers to an agent that comprises an amino acid sequence which has been altered by the introduction of amino acid residue substitutions, deletions, and/or additions. The term "derivative" as used herein also refers to an agent which has been modified, i.e., by the covalent attachment of any type of molecule to the agent. For example, but not by way of limitation, an antibody may be modified, e.g., by glycosylation, acetylation, pegylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to a cellular ligand or other protein, etc. A derivative of an agent may be produced by chemical modifications using techniques known to those of skill in the art, including, but not limited to specific chemical cleavage, acetylation, formylation, metabolic synthesis of tunicamycin, etc. Further, a derivative of an agent may contain one or more non-classical amino acids. A derivative of an agent possesses a similar or identical function as the agent from which it was derived.

As used herein, the term "about" or "approximately" when used in conjunction with a number refers to any number within 1, 5 or 10% of the referenced number.

As used herein, the term "effective amount" in the context of administering a therapy to a subject refers to the amount of a therapy which has a prophylactic and/or therapeutic effect(s). In certain embodiments, in the context of administration of a therapy to a subject, "effective amount" refers to the amount of a therapy which is sufficient to achieve one, two, three, four, or more of the following effects: (i) reduction or amelioration in the severity of FmoPV infection, a FmoPV disease or symptom associated therewith; (ii) reduction in the duration of FmoPV infection, a FmoPV disease or symptom associated therewith; (iii) prevention of the progression of a FmoPV infection, a FmoPV disease or symptom associated therewith; (iv) regression of a FmoPV infection, a FmoPV disease or symptom associated therewith; (v) prevention of the development or onset of a FmoPV infection, a FmoPV disease or symptom associated therewith; (vi) prevention of the recurrence of a FmoPV infection, a FmoPV disease or symptom associated therewith; (vii) reduction or prevention of the spread of a FmoPV from one cell to another cell, one tissue to another tissue, or one organ to another organ; (viii) prevention or reduction of the spread/transmission of a FmoPV from one subject to another subject; (ix) reduction in organ failure associated with a FmoPV infection or FmoPV disease; (x) reduction in the hospitalization of a subject; (xi) reduction in the hospitalization length; (xii) an increase in the survival of a subject with a FmoPV infection or a disease associated therewith; (xiii) elimination of a FmoPV infection

or a disease associated therewith; (xiv) inhibition or reduction in FmoPV replication; (xv) inhibition or reduction in the binding or fusion of FmoPV to a host cell(s); (xvi) inhibition or reduction in the entry of an FmoPV into a host cell(s); (xvii) inhibition or reduction of the replication of the FmoPV genome; (xviii) inhibition or reduction in the synthesis of FmoPV proteins; (xix) inhibition or reduction in the assembly of FmoPV particles; (xx) inhibition or reduction in the release of FmoPV particles from a host cell(s); (xxi) reduction in FmoPV titer; (xxii) reduction in the number of symptoms associated with a FmoPVB infection or a FmoPV disease; (xxiii) enhancement, improvement, supplementation, complementation, or augmentation of the prophylactic or therapeutic effect(s) of another therapy; (xxiv) prevention of the onset or progression of a secondary infection associated with a FmoPV infection; and/or (xxv) prevention of the onset or diminution of disease severity of occurring secondary to FmoPV infections. Exemplary doses of an effective amount are provided herein below.

In certain embodiments, the effective amount of a therapy does not result in complete protection from a FmoPV disease, but results in a lower titer or reduced number of FmoPV compared to an untreated subject. In certain embodiments, the effective amount of a therapy results in a 0.5 fold, 1 fold, 2 fold, 4 fold, 6 fold, 8 fold, 10 fold, 15 fold, 20 fold, 25 fold, 50 fold, 75 fold, 100 fold, 125 fold, 150 fold, 175 fold, 200 fold, 300 fold, 400 fold, 500 fold, 750 fold, or 1,000 fold or greater reduction in titer of FmoPV relative to an untreated subject. In certain embodiments, the effective amount of a therapy results in a reduction by 0.5 log, 1 log, 2 logs, 3 logs, 4 logs, 5 logs, 6 logs, 7 logs, or 10 logs or more in titer of FmoPV relative to an untreated subject. Benefits of a reduction in the titer, number or total burden of FmoPV include, but are not limited to, less severe symptoms of the infection, fewer symptoms of the infection, reduction in the length of the disease associated with the infection, and prevention of the onset or diminution of disease severity of infection occurring secondary to FmoPV infections.

As used herein, the term "fragment" in the context of a nucleic acid sequence refers to a nucleotide sequence comprising at least 2 or at least 3 consecutive nucleotides from a parent sequence. In a specific embodiment, the term refers to a nucleotide sequence of 2 to 30, 5 to 30, 10 to 60, 25 to 100, 150 to 300 or more consecutive nucleotides from a parent sequence. In another embodiment, the term refers to a nucleotide sequence of at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 125, 150, 175, 200, 250, 275, 300, 325, 350, 375, 400, 425, 450 or 475 consecutive nucleotides of a parent sequence.

As used herein, the term "fragment" in the context of an amino acid sequence refers to an amino acid sequence comprising at least 2 consecutive amino acid residues from a parent sequence. In a specific embodiment, the term refers to an amino acid sequence of 2 to 30, 5 to 30, 10 to 60, 25 to 100, 150 to 300 or more consecutive amino acid residues from a parent sequence. In another embodiment, the term refers to an amino acid sequence of at least 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, 100, 110, 125, 150, 175, 200, 250, 275, 300, 325, 350, 375, 400, 425, 450 or 475 consecutive amino acid residues of a parent sequence.

As used herein, the term "heterologous" refers to a unit that is not found naturally be associated with another unit. For example, a first nucleotide sequence is said be a heterologous to a second nucleotide sequence if the two nucleotide sequences are not found in nature to be associated with each other.

As used herein, the term "host cell" refers to any type of cell, e.g., a primary cell or a cell from a cell line. In specific embodiments, the term "host cell" refers a cell transfected with a nucleic acid molecule and the progeny or potential progeny of such a cell. Progeny of such a cell may not be identical to the parent cell transfected with the nucleic acid molecule due to mutations or environmental influences that may occur in succeeding generations or integration of the nucleic acid molecule into the host cell genome.

As used herein, the term "in combination" in the context of the administration of a therapy(ies) to a subject, refers to the use of more than one therapy. The use of the term "in combination" does not restrict the order in which therapies are administered to a subject. A first therapy can be administered prior to (e.g., 5 minutes, 15 minutes, 30 minutes, 45 minutes, 1 hour, 2 hours, 4 hours, 6 hours, 12 hours, 24 hours, 48 hours, 72 hours, 96 hours, 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 8 weeks, or 12 weeks before), concomitantly with, or subsequent to (e.g., 5 minutes, 15 minutes, 30 minutes, 45 minutes, 1 hour, 2 hours, 4 hours, 6 hours, 12 hours, 24 hours, 48 hours, 72 hours, 96 hours, 1 week, 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 8 weeks, or 12 weeks after) the administration of a second therapy to a subject.

As used herein, the term "infection" means the invasion by, multiplication and/or presence of a virus in a cell or a subject. In one embodiment, an infection is an "active" infection, i.e., one in which the virus is replicating in a cell or a subject. Such an infection is characterized by the spread of the virus to other cells, tissues, and/or organs, from the cells, tissues, and/or organs initially infected by the virus. An infection may also be a latent infection, i.e., one in which the virus is not replicating. In certain embodiments, an infection refers to the pathological state resulting from the presence of the virus in a cell or a subject, or by the invasion of a cell or subject by the virus.

As used herein, the term "FmoPV disease" and phrases referring to a disease associated with a FmoPV infection refer to the pathological state resulting from the presence of a FmoPV in a cell or subject or the invasion of a cell or subject by a FmoPV. In specific embodiments, the term refers to a kidney disease caused by a FmoPV.

As used herein, the term "isolated" in the context of nucleic acids refers to a nucleic acid molecule which is separated from other nucleic acid molecules which are present in the natural source of the nucleic acid molecule. Moreover, an "isolated" nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material, or culture medium when produced by recombinant techniques, or substantially free of chemical precursors or other chemicals when chemically synthesized; however, "isolated" excludes members of a library of clones such as a cDNA library. In a specific embodiment, a nucleic acid described herein is isolated. In another specific embodiment, antibodies described herein are isolated. The language "substantially free of other cellular material" includes preparations of a nucleic acid molecule in which the nucleic acid molecule is separated from cellular components of the cells from which it is isolated or recombinantly produced. Thus, a nucleic acid molecule that is substantially free of cellular material includes preparations having less than about 30%, 20%, 10%, or 5% (by dry weight) of heterologous nucleic acid molecules or other cellular components. When the nucleic acid molecule is recombinantly produced, it is also preferably substantially free of culture medium, i.e., culture medium represents less than about 20%, 10%, or 5% of the volume of the nucleic acid molecule preparation. When the nucleic acid molecule is produced by chemical synthesis, it is preferably substantially free of chemical precursors or other chemicals, i.e., it is separated

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from chemical precursors or other chemicals which are involved in the synthesis of the nucleic acid molecule. Accordingly such preparations of the nucleic acid molecule have less than about 30%, 20%, 10%, 5% (by dry weight) of chemical precursors or compounds other than the nucleic acid molecule of interest.

As used herein, the phrase "multiplicity of infection" or "MOI" is the average number of virus per infected cell. The MOI is determined by dividing the number of virus added (ml added \times plaque forming units (pfu)) by the number of cells added (ml added \times cells/ml).

As used herein, the terms "nucleic acid" and "nucleotides" refer to deoxyribonucleotides, deoxyribonucleic acids, ribonucleotides, and ribonucleic acids, and polymeric forms thereof, and includes either single- or double-stranded forms. In certain embodiments, such terms include known analogues of natural nucleotides, for example, peptide nucleic acids ("PNA's), that have similar binding properties as the reference nucleic acid. In some embodiments, such terms refer to deoxyribonucleic acids (e.g., cDNA or DNA). In other embodiments, such terms refer to ribonucleic acids (e.g., mRNA or RNA).

As used herein, the terms "prevent," "preventing" and "prevention" in the context of the administration of a therapy(ies) to a subject refer to a prophylactic effect that results from the administration of a therapy or a combination of therapies. In a specific embodiment, the terms "prevent," "preventing" and "prevention" in the context of the administration of a therapy(ies) to a subject to prevent a disease refer to one or more of the following effects resulting from the administration of a therapy or a combination of therapies: (i) the inhibition or reduction in the development or onset of a disease or a symptom thereof; (ii) the inhibition or reduction in the recurrence of a disease or a symptom associated therewith; and (iii) the reduction or inhibition in a pathogen infection and/or replication. In other specific embodiment, the terms "prevent," "preventing" and "prevention" in the context of the administration of a therapy(ies) to a subject to prevent a FmoPV disease refer to one or more of the following effects resulting from the administration of a therapy or a combination of therapies: (i) the inhibition or reduction in the development or onset of a FmoPV disease or a symptom thereof; (ii) the inhibition or reduction in the recurrence of a FmoPV disease or a symptom associated therewith; and (iii) the reduction or inhibition in FmoPV infection and/or replication.

In another specific embodiment, the terms "prevent," "preventing" and "prevention" in the context of the administration of a therapy(ies) to a subject to prevent a FmoPV infection refer to one or more of the following effects resulting from the administration of a therapy or a combination of therapies: (i) the reduction or inhibition of the spread of FmoPV from one cell to another cell; (ii) the reduction or inhibition of the spread of FmoPV from one organ or tissue to another organ or tissue; and/or (iii) the reduction or inhibition of the spread of FmoPV from one region of an organ or tissue to another region of the organ or tissue (e.g., the reduction in the spread of FmoPV from the upper to the lower respiratory tract).

As used herein, the terms "subject" and "patient" are used interchangeably to refer to an animal (e.g., cats, dogs, birds, reptiles, and mammals). In a specific embodiment, a subject is a cat. In another embodiment, a subject is a mammal including a non-primate (e.g., a camel, donkey, zebra, cow, pig, horse, goat, sheep, cat, dog, rat, and mouse) and a primate (e.g., a monkey, chimpanzee, and a human). In another embodiment, a subject is a non-human mammal. In another embodiment, a subject is a human.

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As used herein, the terms "therapies" and "therapy" can refer to any protocol(s), method(s), compound(s), composition(s), formulation(s), and/or agent(s) that can be used in the prevention or treatment of a viral infection or a disease or symptom associated therewith. In certain embodiments, the terms "therapies" and "therapy" refer to biological therapy, supportive therapy, and/or other therapies useful in treatment or prevention of a viral infection or a disease or symptom associated therewith known to one of skill in the art. In some embodiments, the term "therapy" refers to an immunogenic composition (e.g., a FmoPV vaccine).

As used herein, the terms "treat," "treatment," and "treating" in the context of the administration of a therapy(ies) to a subject refer a beneficial or therapeutic effect resulting from the administration of a therapy or a combination of therapies. In specific embodiments, such terms refer to one, two, three, four, five or more of the following effects resulting from the administration of a therapy or a combination of therapies: (i) reduction or amelioration in the severity of a disease or a symptom associated therewith; (ii) reduction in the duration of a disease or a symptom associated therewith; (iii) prevention of the progression of a disease or symptom associated therewith; (iv) regression of a disease or a symptom associated therewith; (v) prevention of the development or onset of a disease or a symptom associated therewith; (vi) prevention of the recurrence of a disease or a symptom associated therewith; (vii) reduction or prevention of the spread of a pathogen from one cell to another cell, one tissue to another tissue, or one organ to another organ; (viii) prevention or reduction of the spread/transmission of a pathogen from one subject to another subject; (ix) reduction in organ failure associated with a disease; (x) reduction in the hospitalization of a subject; (xi) reduction in the hospitalization length; (xii) an increase in the survival of a subject with a disease associated therewith; (xiii) elimination of a disease; (xiv) inhibition or reduction in pathogen replication; (xv) reduction in pathogen numbers; (xvi) the reduction in the number of symptoms associated with a disease; and (xvi) enhancement, improvement, supplementation, complementation, or augmentation of the prophylactic or therapeutic effect(s) of another therapy.

As used herein, in some embodiments, the term "wild-type" in the context of a virus refers to the types of viruses that are prevalent, circulating and naturally producing typical outbreaks of disease.

4. BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 shows the genome organization of FmoPV and other *morbilliviruses*. The genes are shown as boxes that are drawn to scale. For the P gene, the first line above the box labeled "P" with the letter V at the end of the line represents the region of V CDS and the second line with the letter C at the end of the line represents the C CDS.

FIGS. 2-1 to 2-10 indicate the 16050 bp nucleotide sequence of FmoPV 761U Cats/Hong Kong/2009 (SEQ ID NO: 1).

FIGS. 3-1 to 3-10 indicate the 16050 bp nucleotide sequence of FmoPV 776U Cats/Hong Kong/2009 (SEQ ID NO: 2).

FIGS. 4-1 to 4-10 indicate the 16050 bp nucleotide sequence of FmoPV M252A Cats/Hong Kong/2009 (SEQ ID NO: 3).

FIG. 5 Multiple alignments of N proteins of FmoPV and other *morbilliviruses* (SEQ ID NOS 9, 7-8 and 21-26, respectively, in order of appearance). The conserved MA(S,T)L motif in *morbilliviruses* and the three conserved motifs in *paramyxoviruses* are marked in open boxes with solid line

border and reported consensus sequences (SEQ ID NOS 27-28, respectively, in order of appearance) are indicated above the alignment (where x represents any amino acid residue and Ø represents an aromatic amino acid residue). Amino acid residue numbers for each protein are shown to the right of each sequence. Dots indicate identical residues and dashes indicate gaps. The NES are in open boxes with dotted line border and the NLS in open box with dashed line border.

FIGS. 6A-D indicate four panels. Panel A shows the cytopathic effects of FmoPV on CRFK cells. The open squares show the formation of giant cells. Panels B and C, show indirect immunofluorescent antigen detection in uninfected and infected CRFK cells using serum from guinea pig immunized with recombinant N protein of FmoPV, showing specific apple green cytoplasmic fluorescence in FmoPV infected CRFK cells. Panel D is an electron microscopic examination of infected CRFK cell culture supernatant showing enveloped virus with burst envelope and typical "herring bone" appearance of helical N in *paramyxoviruses*.

FIGS. 7A-F are phylogenetic analyses of the N, P, M, F, A and L amino acid sequences of FmoPV. The trees were constructed by maximum likelihood method with bootstrap values calculated from 1000 trees and rooted on midpoint. The scale bars indicate the branch length that corresponds to 0.5 substitutions per site. Three strains from FmoPV were named as 761U, 776U, M252A. Names and accession numbers of the other viruses are listed in Table 3.

FIG. 8 is a phylogenetic analysis of amino acid sequences of 72-bp fragment of L gene of *paramyxoviruses* identified from cats in the present study. The tree was constructed by neighbor-joining method. The scale bar indicates the branch length that corresponds to 2 amino acid differences per sequence. The three strains from stray cats numbered 761U, 776U and M252A with genome sequences determined are shown in bold. RSV, respiratory syncitial virus (U39661); DmoPV, Dolphin *morbillivirus* (NC_005283); PprPV, *Peste-des-petits ruminants virus* (NC_006383); MeaPV, Measles virus (NC_001498); CdipV, Canine distemper virus (NC_001921); MosPV, Mossman virus (NC_005339); NarPV, Nariva virus (FJ362497); ThkPV3, *Tuhoko* virus 3 (GU128082); ThkPV2, *Tuhoko* virus 2 (GU128081); ThkPV, *Tuhoko* virus 1 (GU128080); JPV, J-virus (NC_007454); BeiPV, Beilong virus (NC_007803); NipPV, Nipah virus (NC_002728); HenPV, Hendra virus (NC_001906); Fd1PV, Fer-de-lance virus (NC_005084); SenPV, Sendai virus (NC_001552); HpiPV-1, Human parainfluenza virus 1 (NC_003461).

FIG. 9 shows a Western blot analysis with stray cat sera against the purified (His)₆-tagged ("(His)6" disclosed as SEQ ID NO: 10) recombinant FmoPV N protein antigen. Results of RT-PCR of the corresponding urine samples for FmoPV are also shown.

FIGS. 10A-F indicate six panels. Panels A and B show histological section of kidneys stained by H & E from a stray cat with FmoPV detected in urine and a normal cat, showing aggregates of inflammatory cells in the interstitium and renal tubular degeneration in the infected cat. Panels C and D show immunohistochemical staining of kidney sections of a stray cat with FmoPV detected in urine using guinea pig serum positive for anti-FmoPV N protein antibody and preimmune guinea pig serum, showing positive renal tubular cells. Panels E and F show immunohistochemical staining of lymph node sections of a stray cat positive for FmoPV using guinea pig serum positive for anti-FmoPV N protein antibody and pre-immune guinea pig serum, showing positive mononuclear cells.

FIGS. 11A-B present representative images of cauxin-immunohistochemical stained paraffin-embedded renal sections of cats without and with histological evidence of TIN in Panels A and B, respectively.

FIGS. 12A-C show double staining of the lymph node of an FmoPV infected stray cat for (A) mouse anti-human myeloid/histocyte antigen and then labeled with Texas-red conjugated goat anti-mouse IgG; (B) guinea pig antiserum against the N protein of FmoPV, followed by FITC conjugated rabbit anti-guinea pig IgG; (C) the merged photo showed that both antigens co-localized in cytoplasm of the cells.

FIG. 13 shows the N protein polypeptide comprising the sequence of 776U, M252A, and 761U, which is used as an antigenic peptide.

5. DETAILED DESCRIPTION OF THE INVENTION

5.1 Nucleic Acids

In one aspect, provided herein are nucleic acid sequences comprising or consisting of a wild-type or a modified feline *morbillivirus* ("FmoPV"). Also provided are modified FmoPV gene segment (genomic RNA) or the complement thereof (antigenomic RNA).

In one aspect, described herein is the entire nucleotide sequence of the FmoPV. In certain embodiments, the nucleotide sequences are Genbank accession numbers: JQ411014, JQ411015 and JQ411016. The JQ411014 nucleotide sequence is shown in FIG. 2, labeled as FmoPV 761U Cats/Hong Kong/2009. The JQ411015 nucleotide sequence is shown in FIG. 3, labeled as FmoPV 776U Cats/Hong Kong/2009. The JQ411016 nucleotide sequence is shown in FIG. 4, labeled as FmoPV M252A Cats/Hong Kong/2009.

In other aspects, described herein are a complement, analog, derivative, or fragment thereof, or a portion of the FmoPV nucleotide sequence. In certain embodiments, described herein are nucleic acid molecules that hybridizes to any portion of the genome of the FmoPV, under stringent conditions. In specific embodiment, described herein are nucleic acid molecules which are suitable for use as primers consisting of or comprising the nucleic acid sequence of the FmoPV. In another embodiment, described herein are nucleic acid molecules that are suitable for use as hybridization probes for the detection of FmoPV. The primers and probes are contained in a kit for the detection of nucleic acid molecules or proteins from wild-type, natural or artificial variants, analogs, or derivatives of FmoPV.

Described herein is a natural variant of FmoPV having a sequence that is different from the genomic sequence of Genbank accession numbers: JQ411014, JQ411015 and JQ411016 due to one or more naturally occurred mutations, including, but not limited to, point mutations, rearrangements, insertions, deletions, etc., to the genomic sequence that may or may not result in a phenotypic change. Preferably, the variants include 1-5, 6-10, 11-10, 20-40, 40-60, 60-100, 100-500, 500-1000, 1000-2000 nucleic acid changes in the genome. In certain embodiments, the mutation of the genomic sequence of the FmoPV resulted in rearrangements, insertions, and/or deletions relative to the wild-type genomic sequence of FmoPV.

In certain embodiments, a nucleic acid sequence described herein is part of or incorporated into a vector. In a specific embodiment, a nucleic acid sequence described herein is part of or incorporated into a vector that facilitates the production of a modified FmoPV gene segment or the complement thereof. In one embodiment, a nucleic acid sequence

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described herein is part of or incorporated into the pDZ vector (see, e.g., Quinlivan et al., 2005, *J. of Virology* 79: 8431-8439 for information relating to the pDZ vector). In another embodiment, a nucleic acid sequence described herein is part of or incorporated into the pHW2000 vector (see, e.g., Hoffmann et al., 2000, *Proc Natl Acad Sci USA*. 97(11):6108-13 for information relating to the pHW2000 vector). In another embodiment, a nucleic acid sequence described herein is part of or incorporated into the pAD3000 vector (see, e.g., Hoffmann et al., 2000, *Proc Natl Acad Sci USA*. 97(11):6108-13 for information relating to the pAD3000 vector). In another embodiment, a nucleic acid sequence described herein is part of or incorporated into the pAD4000 vector (see, e.g., Wang et al., 2007, *J. of Virology* 4: 102 for information relating to the pAD4000 vector). In one embodiment, a nucleic acid sequence described herein is part of or incorporated into the vector in Section 6 infra.

Techniques for the production or use of the nucleic acids will employ, unless otherwise indicated, routine conventional techniques of molecular biology and recombinant DNA manipulation and production. Any cloning technique known to the skilled artisan can be used to assemble the nucleic acids described herein and to mutate nucleotides where necessary. Such techniques are well-known and are available to the skilled artisan in laboratory manuals such as Sambrook and Russell, *Molecular Cloning: A Laboratory Manual*, 3rd edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (2001). In particular, polymerase chain reaction, restriction enzymes, ligase enzyme, mutagenic primers, and amplification of nucleic acid fragments in vectors can be used to generate the individual elements of the nucleic acids described herein and then to assemble them.

In some embodiments, a nucleic acid sequence described herein is introduced (e.g., transfected) into a substrate, such as a host cell or an embryonated egg. Thus, in some embodiments, provided herein is a substrate (e.g., host cells or eggs) comprising a nucleic acid sequence described herein. In other embodiments, a nucleic acid sequence described herein that is part of or incorporated into a vector is introduced (e.g., transfected) into a substrate, such as a host cell or an embryonated egg. Thus, in some embodiments, provided herein is a substrate (e.g., host cells or eggs) comprising a nucleic acid sequence described herein that is part of or incorporated into a vector. In certain embodiments, provided herein is a cell line that is transformed with the vector containing FmoPV nucleic acid sequences. In certain embodiments, provided herein is a transgenic animal containing a vector comprising FmoPV nucleic acid sequences.

In certain embodiments, the FmoPV nucleic acid is used in a diagnostic assay for the FmoPV infection. In particular, the diagnostic assay is a quantitative assay for the detection of the FmoPV, natural or artificial variants, analogs, or derivatives thereof. In certain embodiments, the quantitative assay is PCR or RT-PCR. In certain embodiments, the FmoPV nucleic acid is in separate containers in a diagnostic kit. In specific embodiments, the nucleic acid that encodes a portion or fragment of any gene of FmoPV, natural or artificial variants, analogs, or derivatives thereof, can be used as a target for diagnostic purpose. In a specific embodiment, the nucleic acid that encodes the L gene of FmoPV is used as target for diagnosis. In one specific embodiment, diagnosis is made by amplifying a 172 bp L gene fragment from a cDNA template using quantitative PCR system. In a specific embodiment, the primers (LPW124905'-CAGAGACTTAATGAAATT-TATGG-3'; LPW124915'-CCACCCATCGGTTACTT-3' (SEQ ID NO: 12)) are used. Sequences of target fragments are shown in FIG. 13.

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5.2 Proteins

The open reading frames of FmoPV gene segments can be determined using standard molecular biology and virology techniques. Provided herein are FmoPV polypeptides expressed by the FmoPV nucleic acid molecule comprising the FmoPV nucleic acid sequences. In certain embodiments, the FmoPV proteins are. In certain embodiments, FmoPV antigens are fragments or full length N, P/V/C(P), P/V/C(V), P/V/C(C), M, F, H and L proteins. Also described herein are recombinant or chimeric viruses encoded by viral vectors derived from the genome of FmoPV or natural variants thereof.

In another specific embodiment, described herein is a chimeric FmoPV virus which further comprises a heterologous nucleotide sequence. In certain embodiments, a chimeric virus may be encoded by a nucleotide sequence in which heterologous nucleotide sequences have been added to the genome or in which endogenous or native nucleotide sequences have been replaced with heterologous nucleotide sequences.

In certain embodiments, the chimeric viruses are encoded by the vectors which further comprise a heterologous nucleotide sequence. In accordance with the present invention a chimeric virus is encoded by a viral vector that may or may not include nucleic acids that are non-native to the viral genome. In accordance with the invention a chimeric virus is encoded by a viral vector to which heterologous nucleotide sequences have been added, inserted or substituted for native or non-native sequences. In accordance with the present invention, the chimeric virus may be encoded by nucleotide sequences derived from different strains or variants of FmoPV. In particular, the chimeric virus is encoded by nucleotide sequences that encode antigenic polypeptides derived from different strains or variants of FmoPV.

A chimeric virus may be of particular use for the generation of recombinant vaccines protecting against two or more viruses (Tao et al., *J. Virol.* 72:2955-2961; Durbin et al., 2000, *J. Virol.* 74:6821-6831; Skiadopoulos et al., 1998, *J. Virol.* 72:1762-1768; Teng et al., 2000, *J. Virol.* 74:9317-9321). For example, it can be envisaged that a vector expressing one or more proteins of FmoPV and FmoPV variants, will protect a subject vaccinated with such vector against infections by both the FmoPV and FmoPV variant. Attenuated and replication-defective viruses may be of use for vaccination purposes with live vaccines.

In accordance with the present invention the heterologous sequence to be incorporated into the viral vectors encoding the recombinant or chimeric viruses of the invention include sequences obtained or derived from different strains or variants of the FmoPV.

In certain embodiments, the chimeric or recombinant viruses of the invention are encoded by viral vectors derived from viral genomes wherein one or more sequences, intergenic regions, termini sequences, or portions or entire ORF have been substituted with a heterologous or non-native sequence. In certain embodiments of the invention, the chimeric viruses of the invention are encoded by viral vectors derived from viral genomes wherein one or more heterologous sequences have been inserted or added to the vector.

Any nucleotide sequence heterologous to FmoPV may be included in a modified FmoPV gene segment described herein. In certain embodiments, the heterologous nucleotide sequence is 8 to 100 nucleotides in length, 15 to 100 nucleotides in length, 25 to 100 nucleotides in length, 50 to 200 nucleotide in length, 50 to 400 nucleotide in length, 200 to 500 nucleotide in length, or 400 to 600 nucleotides in length,

500 to 800 nucleotide in length. In other embodiments, the heterologous nucleotide sequence is 750 to 900 nucleotides in length, 800 to 100 nucleotides in length, 850 to 1000 nucleotides in length, 900 to 1200 nucleotides in length, 1000 to 1200 nucleotides in length, 1000 to 1500 nucleotides or 10 to 1500 nucleotides in length. In some embodiments, the heterologous nucleotide encodes a peptide or polypeptide that is 5 to 10 amino acids in length, 10 to 25 amino acids in length, 25 to 50 amino acids in length, 50 to 100 amino acids in length, 100 to 150 amino acids in length, 150 to 200 amino acids in length, 200 to 250 amino acids in length; 250 to 300 amino acids in length, 300 to 400 amino acids in length, or 500 or more amino acids in length. In some embodiments, the heterologous nucleotide encodes a polypeptide that does not exceed 500 amino acids in length. In specific embodiments the heterologous nucleotide sequence does not contain a stop codon. In certain embodiments, the heterologous nucleotide sequence is codon-optimized. Techniques for codon optimization are known in the art and can be applied to codon optimize a heterologous nucleotide sequence.

In one embodiment, a heterologous nucleotide sequence encodes an antigen of any infectious pathogen or an antigen associated with any disease that is capable of eliciting an immune response. In a specific embodiment, the antigen is a glycoprotein. In certain embodiments, a heterologous nucleotide sequence encodes a viral antigen. In other embodiments, the viral antigen is an antigen from a virus other than a FmoPV.

In specific embodiments, a FmoPV described herein is attenuated. In a particular embodiment, the FmoPV is attenuated such that the virus remains, at least partially, infectious and can replicate in vivo, but only generate low titers resulting in subclinical levels of infection that are non-pathogenic. Such attenuated viruses are especially suited for embodiments described herein wherein the virus or an immunogenic composition thereof is administered to a subject to induce an immune response.

In some embodiments, a FmoPV described herein comprises one or more attenuating mutations in a modified FmoPV gene segment. In some embodiments, a FmoPV described herein comprises one or more attenuating mutations in a complementing FmoPV gene segment. In certain embodiments, a FmoPV described herein comprises one or more attenuating mutations in two, three or more complementing FmoPV gene segments. In some embodiments, a FmoPV described herein comprises one or more attenuating mutations in a modified FmoPV gene segment and one or more attenuating mutations in a complementing FmoPV gene segment.

The selection of the viral vector may depend on the species of the subject that is to be treated or protected from a viral infection. If the subject is a feline, then an attenuated FmoPV can be used to provide the antigenic sequences.

In accordance with the present invention, the viral vectors can be engineered to provide antigenic sequences which confer protection against infection by the FmoPV, natural or artificial variants, analogs, or derivatives thereof. The viral vectors may be engineered to provide one, two, three or more antigenic sequences. In accordance with the present invention the antigenic sequences may be derived from the same virus, from different strains or variants of the same type of virus, or from different viruses.

The expression products and/or recombinant or chimeric virions obtained in accordance with the invention may advantageously be utilized in vaccine formulations. The expression products and chimeric virions of may be engineered to create vaccines against a broad range of pathogens, including viral

and bacterial antigens, tumor antigens, allergen antigens, and auto antigens involved in autoimmune disorders. In particular, the chimeric virions of the present invention may be engineered to create vaccines for the protection of a subject from infections with the FmoPV, natural or artificial variants, analogs, or derivatives thereof.

In another aspect, the mutation of the genomic sequence of the FmoPV resulted in changes in the FmoPV proteins. In certain embodiments, the mutation of the genomic sequence of the FmoPV resulted in less than 25, 20, 15, 10, 5, 4, 3, or 2 amino acid substitutions in the FmoPV proteins.

Either conservative or non-conservative amino acid substitutions can be made at one or more amino acid residues. In preferred embodiments, the variants have conservative amino acid substitutions that are made at one or more predicted non-essential amino acid residues (i.e., amino acid residues which are not critical for the expression of the biological activities of the virus, e.g., infectivity, replicability, protein synthesis ability, assembling ability, and cytotoxic effect). In other embodiments, the variants have non-conservative amino acid substitutions that are made at one or more predicted non-essential amino acid residues (i.e., amino acid residues which are not critical for the biological activities of the virus, e.g., infectivity, replication ability, protein synthesis ability, assembling ability, and cytotoxic effect). In other embodiments, the amino acid substitutions are made at essential amino acid residues (i.e., amino acid residues which are critical for the biological activities of the virus, e.g., infectivity, replicability, protein synthesis ability, assembling ability, and cytotoxic effect).

A “conservative amino acid substitution” is one in which the amino acid residue is replaced with an amino acid residue having a side chain with a similar charge. A “non-conservative amino acid substitution” is one in which the amino acid residue is replaced with an amino acid residue having a side chain with an opposite charge. Families of amino acid residues having side chains with similar charges have been defined in the art. Genetically encoded amino acids can be divided into four families: (1) acidic=aspartate, glutamate; (2) basic=lysine, arginine, histidine; (3) nonpolar=alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan; and (4) uncharged polar=glycine, asparagine, glutamine, cysteine, serine, threonine, tyrosine. In similar fashion, the amino acid repertoire can be grouped as (1) acidic=aspartate, glutamate; (2) basic=lysine, arginine, histidine, (3) aliphatic=glycine, alanine, valine, leucine, isoleucine, serine, threonine, with serine and threonine optionally be grouped separately as aliphatic-hydroxyl; (4) aromatic=phenylalanine, tyrosine, tryptophan; (5) amide=asparagine, glutamine; and (6) sulfur-containing=cysteine and methionine. (See, for example, Biochemistry, 4th ed., Ed. by L. Stryer, WH Freeman and Co.: 1995).

The invention further relates to mutant FmoPV peptides. In one embodiment, mutations can be introduced randomly along all or part of the coding sequence of the FmoPV or variants thereof, such as by saturation mutagenesis, and the resultant mutants can be screened for biological activity to identify mutants that retain activity. Techniques for mutagenesis known in the art can also be used, including but not limited to, point-directed mutagenesis, chemical mutagenesis, in vitro site-directed mutagenesis, using, for example, the QuikChange Site-Directed Mutagenesis Kit (Stratagene), etc. Non-limiting examples of such modifications include substitutions of amino acids to cysteines toward the formation of disulfide bonds; substitution of amino acids to tyrosine and subsequent chemical treatment of the polypeptide toward the

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formation of dityrosine bonds, as disclosed in detail herein; one or more amino acid substitutions and/or biological or chemical modification toward generating a binding pocket for a small molecule (substrate or inhibitor), and/or the introduction of side-chain specific tags (e.g., to characterize molecular interactions or to capture protein-protein interaction partners). In a specific embodiment, the biological modification comprises alkylation, phosphorylation, sulfation, oxidation or reduction, ADP-ribosylation, hydroxylation, glycosylation, glucosylphosphatidylinositol addition, ubiquitination. In another specific embodiment, the chemical modification comprises altering the charge of the recombinant virus. In yet another embodiment, a positive or negative charge is chemically added to an amino acid residue where a charged amino acid residue is modified to an uncharged residue.

5.3 Construction of Recombinant FmoPV

Techniques known to one skilled in the art may be used to produce a recombinant FmoPV containing a modified FmoPV gene segment described herein. For example, reverse genetics techniques may be used to generate such a FmoPV. Briefly, reverse genetics techniques generally involve the preparation of synthetic recombinant viral RNAs that contain the non-coding regions of the negative-strand, viral RNA which are essential for the recognition by viral polymerases and for packaging signals necessary to generate a mature virion. The recombinant RNAs are synthesized from a recombinant DNA template and reconstituted in vitro with purified viral polymerase complex to form recombinant ribonucleoproteins (RNPs) which can be used to transfect cells. A more efficient transfection is achieved if the viral polymerase proteins are present during transcription of the synthetic RNAs either in vitro or in vivo. The synthetic recombinant RNPs can be rescued into infectious virus particles.

Alternatively, helper-free plasmid technology may be used to produce a recombinant FmoPV containing a modified FmoPV gene segment. Briefly, full length cDNAs of viral segments are amplified using PCR with primers that include unique restriction sites, which allow the insertion of the PCR product into the plasmid vector. The plasmid vector is designed so that an exact negative (vRNA sense) transcript is expressed. For example, the plasmid vector may be designed to position the PCR product between a truncated human RNA polymerase I promoter and a hepatitis delta virus ribozyme sequence such that an exact negative (vRNA sense) transcript is produced from the polymerase I promoter. Separate plasmid vectors comprising each viral segment as well as expression vectors comprising necessary viral proteins may be transfected into cells leading to production of recombinant viral particles. In another example, plasmid vectors from which both the viral genomic RNA and mRNA encoding the necessary viral proteins are expressed may be used.

5.4. Propagation of FmoPV

The FmoPV described herein can be propagated in any substrate that allows the virus to grow to titers that permit the uses of the viruses described herein. In one embodiment, the substrate allows the FmoPV described herein to grow to titers comparable to those determined for the corresponding wild-type viruses.

The FmoPV described herein may be grown in host cells (e.g., cat, avian cells, chicken cells, etc.) that are susceptible to infection by the viruses, embryonated eggs or animals (e.g., birds). Specific examples of host cells include Vero cells, MDCK cells, MBCK cells, COS cells, 293 cells, 293T cells,

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A549 cells, MDBK cells, etc. Such methods are well-known to those skilled in the art. In a specific embodiment, the FmoPV described herein may be propagated in cell lines. In another embodiment, the FmoPV described herein described herein are propagated in chicken cells or embryonated eggs. Representative chicken cells include, but are not limited to, chicken embryo fibroblasts and chicken embryo kidney cells.

For virus isolation, the FmoPV described herein can be removed from cell culture and separated from cellular components, typically by well known clarification procedures, e.g., such as gradient centrifugation and column chromatography, and may be further purified as desired using procedures well known to those skilled in the art, e.g., plaque assays.

5.5 Compositions & Routes of Administration

The FmoPV described herein may be incorporated into compositions. In a specific embodiment, the compositions are pharmaceutical compositions, such as immunogenic compositions (e.g., vaccine formulations). The pharmaceutical compositions provided herein can be in any form that allows for the composition to be administered to a subject. In a specific embodiment, the pharmaceutical compositions are suitable for veterinary and/or human administration. The compositions may be used in methods of preventing and/or treating an FmoPV infection. The compositions may also be used in methods or preventing and/or treating FmoPV disease. The composition may be used in methods of eliciting an immune response to a particular antigen(s) or in methods of delivering a certain protein to a subject.

In one embodiment, a pharmaceutical composition comprises a FmoPV in an admixture with a pharmaceutically acceptable carrier. In some embodiments, a pharmaceutical composition may comprise one or more other therapies in addition to a FmoPV. In specific embodiments, a FmoPV described herein that is incorporated into a pharmaceutical composition (e.g., an immunogenic composition such as a vaccine) is a live virus. An immunogenic composition comprising a live FmoPV for administration to a subject may be preferred because multiplication of the virus in the subject may lead to a prolonged stimulus of similar kind and magnitude to that occurring in natural infections, and therefore, confer substantial, long lasting immunity.

In some embodiments, a FmoPV described herein that is incorporated into a pharmaceutical composition (e.g., an immunogenic composition such as a vaccine) is inactivated. Techniques known to one of skill in the art may be used to inactivate FmoPV described herein.

In specific embodiments, immunogenic compositions described herein are monovalent formulations. In other embodiments, immunogenic compositions described herein are multivalent formulations.

As used herein, the term "pharmaceutically acceptable" means approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeiae for use in animals, and more particularly in humans. The term "carrier" refers to a diluent, adjuvant, excipient, or vehicle with which the pharmaceutical composition is administered. Saline solutions and aqueous dextrose and glycerol solutions can also be employed as liquid carriers, particularly for injectable solutions. Suitable excipients include starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol and the

like. Examples of suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E. W. Martin.

In certain embodiments, biodegradable polymers, such as ethylene vinyl acetate, polyanhydrides, polyethylene glycol (PEGylation), polymethyl methacrylate polymers, polylactides, poly(lactide-co-glycolides), polyglycolic acid, collagen, polyorthoesters, and polylactic acid, may be used as carriers. Liposomes or micelles can also be used as pharmaceutically acceptable carriers. These can be prepared according to methods known to those skilled in the art, for example, as described in U.S. Pat. No. 4,522,811.

In a specific embodiment, pharmaceutical compositions are formulated to be suitable for the intended route of administration to a subject. For example, the pharmaceutical composition may be formulated to be suitable for parenteral, oral, intradermal, intranasal, transdermal, pulmonary, colorectal, intraperitoneal, and rectal administration. In a specific embodiment, the pharmaceutical composition may be formulated for intravenous, oral, intraperitoneal, intranasal, intratracheal, subcutaneous, intramuscular, topical, intradermal, transdermal or pulmonary administration.

In certain embodiments, the compositions described herein comprise, or are administered in combination with, an adjuvant. The adjuvant for administration in combination with a composition described herein may be administered before, concomitantly with, or after administration of the composition. In specific embodiments, an inactivated virus immunogenic composition described herein comprises one or more adjuvants. In some embodiments, the term "adjuvant" refers to a compound that when administered in conjunction with or as part of a composition described herein augments, enhances and/or boosts the immune response to a FmoPV virus, but when the compound is administered alone does not generate an immune response to the virus. In some embodiments, the adjuvant generates an immune response to a FmoPV and does not produce an allergy or other adverse reaction. Adjuvants can enhance an immune response by several mechanisms including, e.g., lymphocyte recruitment, stimulation of B and/or T cells, and stimulation of macrophages.

Specific examples of adjuvants include, but are not limited to, aluminum salts (alum) (such as aluminum hydroxide, aluminum phosphate, and aluminum sulfate), 3 De-O-acylated monophosphoryl lipid A (MPL) (see GB 2220211) and QS21 (see Kensil et al., in Vaccine Design: The Subunit and Adjuvant Approach (eds. Powell & Newman, Plenum Press, NY, 1995); U.S. Pat. No. 5,057,540). In some embodiments, the adjuvant is Freund's adjuvant (complete or incomplete). Other adjuvants are oil in water emulsions (such as squalene or peanut oil), optionally in combination with immune stimulants, such as monophosphoryl lipid A (see Stoute et al., N. Engl. J. Med. 336, 86-91 (1997)). Another adjuvant is CpG (Bioworld Today, Nov. 15, 1998). Such adjuvants can be used with or without other specific immunostimulating agents such as MPL or 3-DMP, polymeric or monomeric amino acids such as polyglutamic acid or polylysine.

The pharmaceutical compositions described herein can be included in a container, pack, or dispenser together with instructions for administration.

In a particular embodiment, the recombinant N proteins of the present invention have antigenicity, making them suitable for use in immunogenic compositions. The antigenicity of these recombinant N proteins is demonstrated in Example 7. Among tested sera from the 56 cats that were RT-PCR positive and 401 cats that were RT-PCR negative for FmoPV, 49 (76.7%) and 78 (19.4%), respectively, were positive for IgG against N protein of FmoPV by Western blot analysis

($P<0.0001$). See FIG. 9 and see Table 6 below. Among tested sera from the 56 cats that were RT-PCR positive for FmoPV, only 5 (8.9%) were positive for IgM against N protein of FmoPV.

- 5 In one embodiment, a sequence for use as an antigenic peptide is the N protein polypeptide comprising the sequence of 776U, M252A, and 761U as shown in FIG. 13. The antigenic polypeptide is used to detect the presence of FmoPV in a sample.
- 10 In FIG. 9, a Western blot analysis with stray cat sera against the purified (His)₆-tagged ("(His)6" disclosed as SEQ ID NO: 10) recombinant FmoPV N protein antigen, prominent immunoreactive protein bands of about 69 kDa, consistent with the expected size of 68.7 kDa of the recombinant protein, were detected in three of the six cat serum samples shown, indicating antigen-antibody interactions between the recombinant FmoPV N protein and serum antibodies. Results of RT-PCR of the corresponding urine samples for FmoPV are also shown. Table 6 shows the FmoPV viral load and antibody level of RT-PCR positive stray cats in this study.

TABLE 6

Cat no.	Date of sample collection	Type of positive sample(s)	FmoPV	
			Viral load (copies/ml)	Western blot
543	14 May 2009	Urine	1.4×10^4	+
545	14 May 2009	Faecal swab	3.8×10^5	-
557	12 Jun. 2009	Urine	9.5×10^2	+
572	24 Jun. 2009	Urine	1.2×10	+
587	02 Jul. 2009	Urine	4.88	++
591	08 Jul. 2009	Urine	2.7×10^4	+++
592	08 Jul. 2009	Urine	3.0×10^3	+++
670	27 Aug. 2009	Urine	2.7×10^3	+
680	31 Aug. 2009	Urine	8.8×10^3	+++
688	03 Sep. 2009	Urine	7.1×10^3	+++
725	03 Nov. 2009	Faecal swab	2.7×10^3	++
761	24 Nov. 2009	Urine	5.9×10^5	+++
773	01 Dec. 2009	Urine	6.4×10^4	+
776	04 Dec. 2009	Urine	2.3×10^3	+++
802	24 Dec. 2009	Urine	2.76	-
810	29 Dec. 2009	Urine	1.6×10^2	-
818	12 Jan. 2010	Urine	1.06	-
835	22 Jan. 2010	Urine	2.4×10^4	+
850	29 Jan. 2010	Urine	2.1×10^4	++
851	29 Jan. 2010	Urine	2.6	++
		Faecal swab	5.0×10^2	
858	26 Feb. 2010	Urine	6.9×10^4	+
898	23 Mar. 2010	Urine	2.4×10^4	+
900	23 Mar. 2010	Urine	1.6×10^4	+
906	23 Mar. 2010	Urine	9.8×10^3	++
		Faecal swab	2.0×10^4	
908	25 Mar. 2010	Urine	8.8×10^2	+
909	25 Mar. 2010	Urine	2.6×10^3	-
938	29 Apr. 2010	Urine	2.1×10^2	++
962	06 May 2010	Urine	8.0×10^3	+++
968	10 May 2010	Urine	4.7×10^2	+++
970	10 May 2010	Blood	3.1×10^4	+++
979	17 May 2010	Urine	5.3×10^3	+++
990	24 May 2010	Urine	1.4×10^3	++
997	31 May 2010	Urine	5.0×10^3	++
1012	10 Jun. 2010	Urine	9.5×10^3	+
1036	28 Jun. 2010	Urine	1.6×10^4	++
1055	02 Aug. 2010	Urine	1.0×10^3	+
1057	02 Aug. 2010	Urine	9.7×10^3	++
1078	09 Sep. 2010	Urine	2.0×10^5	+
1091	24 Sep. 2010	Urine	7.0×10^3	+
1096	27 Sep. 2010	Urine	2.0×10^4	+++
1107	07 Oct. 2010	Urine	4.6×10^3	++
1148	25 Oct. 2010	Urine	1.4×10^5	++
1155	28 Oct. 2010	Urine	3.2×10^{-1}	+
1189	25 Nov. 2010	Urine	6.9×10^3	+
1226	06 Jan. 2011	Urine	3.7×10^{-2}	+++
1297	28 Feb. 2011	Urine	2.7×10^2	+
1312	09 Mar. 2011	Urine	3.8	++

TABLE 6-continued

Cat no.	Date of sample collection	Type of positive sample(s)	FmoPV	
			Viral load (copies/ml)	Western blot
1314	09 Mar. 2011	Urine	1.6×10^3	-
1325	14 Mar. 2011	Urine	2.3×10^3	++
1327	24 Mar. 2011	Urine	3.7×10^4	+
1336	31 Mar. 2011	Urine	5.4×10^5	++
1357	28 Apr. 2011	Urine	1.0×10^2	++
1359	28 Apr. 2011	Urine	2.0×10^5	+
1392	30 May 2011	Urine	5.2×10^4	-
1407	13 Jun. 2011	Urine	3.5×10	++
1409	16 Jun. 2011	Urine	1.4×10^6	+

Specific apple green finely granular and diffuse cytoplasmic fluorescence was also observed using serum from guinea pig immunized with recombinant N protein of FmoPV or corresponding serum of the infected cat (FIG. 6).

5.6 Immunogenic Compositions Comprising Live Viruses

In one embodiment, provided herein are immunogenic compositions (e.g., vaccines) comprising one or more live FmoPV described herein. In some embodiments, the live virus is attenuated. In some embodiments, an immunogenic composition comprises two, three, four or more live viruses.

In certain embodiments, provided herein are immunogenic compositions (e.g., vaccines) comprising about 10^5 to about 10^{10} fluorescent focus units (FFU) of live attenuated FmoPV described herein, about 0.1 to about 0.5 mg monosodium glutamate, about 1.0 to about 5.0 mg hydrolyzed porcine gelatin, about 1.0 to about 5.0 mg arginine, about 10 to about 15 mg sucrose, about 1.0 to about 5.0 mg dibasic potassium phosphate, about 0.5 to about 2.0 mg monobasic potassium phosphate, and about 0.001 to about 0.05 $\mu\text{g}/\text{ml}$ gentamicin sulfate per dose. In some embodiments, the immunogenic compositions (e.g., vaccines) are packaged as pre-filled sprayers containing single 0.2 ml doses.

In a specific embodiment, provided herein are immunogenic compositions (e.g., vaccines) comprising $10^{6.5}$ to $10^{7.5}$ FFU of live attenuated FmoPV described herein, 0.188 mg monosodium glutamate, 2.0 mg hydrolyzed porcine gelatin, 2.42 mg arginine, 13.68 mg sucrose, 2.26 mg dibasic potassium phosphate, 0.96 mg monobasic potassium phosphate, and <0.015 $\mu\text{g}/\text{ml}$ gentamicin sulfate per dose. In some embodiments, the immunogenic compositions (e.g., vaccines) are packaged as pre-filled sprayers containing single 0.2 ml doses.

In a specific embodiment, the live virus is propagated in embryonated chicken eggs before its use in an immunogenic composition described herein. In another specific embodiment, the live virus is not propagated in embryonated chicken eggs before its use in an immunogenic composition described herein. In another specific embodiment, the live virus is propagated in mammalian cells before its use in an immunogenic composition described herein.

An immunogenic composition comprising a live virus for administration to a subject may be preferred because multiplication of the virus in the subject may lead to a prolonged stimulus of similar kind and magnitude to that occurring in natural infections, and, therefore, confer substantial, long lasting immunity.

5.7 Generation of Antibodies

The FmoPV described herein may be used to elicit antibodies against FmoPV or a heterologous nucleotide

sequence. In a specific embodiment, a FmoPV described herein or a composition thereof may be administered to a non-human subject (e.g., mouse, rabbit, rat, guinea pig, cat, etc.) to induce an immune response that includes the production of antibodies which may be isolated using techniques known to one of skill in the art (e.g., immunoaffinity chromatography, centrifugation, precipitation, etc.).

Alternatively, a virus described herein may be used to screen for antibodies from antibody libraries. For example, a

- 10 FmoPV may be immobilized to a solid support (e.g., a silica gel, a resin, a derivatized plastic film, a glass bead, cotton, a plastic bead, a polystyrene bead, an alumina gel, or a polysaccharide, a magnetic bead), and screened for binding to antibodies. As an alternative, the antibodies may be immobilized
- 15 to a solid support and screened for binding to a FmoPV described herein. Any screening assay, such as a panning assay, ELISA, surface plasmon resonance, or other antibody screening assay known in the art may be used to screen for antibodies that bind to a FmoPV. The antibody library
- 20 screened may be a commercially available antibody library, an in vitro generated library, or a library obtained by identifying and cloning or isolating antibodies from a subject infected with FmoPV. In particular embodiments, the antibody library is generated from a survivor of an FmoPV outbreak.
- 25 Antibody libraries may be generated in accordance with methods known in the art. In a particular embodiment, the antibody library is generated by cloning the antibodies and using them in phage display libraries or a phagemid display library.

- 30 Antibodies elicited or identified in accordance with the methods described herein may be tested for specificity for FmoPV antigens and the ability to neutralize FmoPV using the biological assays known in the art or described herein. In one embodiment, an antibody identified or isolated from a
- 35 non-human animal antibody specifically binds to a FmoPV antigen.

- Antibodies elicited or identified in accordance with the methods described herein may be tested for specificity to, and the ability to neutralize, a peptide or polypeptide antigen encoded by a heterologous nucleotide sequence described
- 40 herein using the biological assays known in the art or described herein. In one embodiment, an antibody identified or isolated from a non-human animal antibody specifically binds to a peptide or polypeptide antigen encoded by a heterologous nucleotide sequence described herein. In one embodiment, the neutralizing antibody neutralizes the viral, bacterial, fungal or other pathogen, or a tumor that expresses the peptide or polypeptide antigen encoded by a heterologous nucleotide sequence described herein.

- 50 Antibodies elicited or identified using a FmoPV described herein include immunoglobulin molecules and immunologically active portions of immunoglobulin molecules, i.e., molecules that contain an antigen binding site that specifically binds to a hemagglutinin polypeptide. The immunoglobulin molecules may be of any type (e.g., IgG, IgE, IgM, IgD, IgA and IgY), class (e.g., IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2) or subclass of immunoglobulin molecule. Antibodies include, but are not limited to, monoclonal antibodies, multispecific antibodies, human antibodies, humanized antibodies, chimeric antibodies, single-chain Fvs (scFv), single chain antibodies, Fab fragments, F(ab') fragments, disulfide-linked Fvs (sdFv), and anti-idiotypic (anti-Id) antibodies (including, e.g., anti-Id antibodies to antibodies elicited or identified using a method described herein), and epitope-binding fragments of any of the above.
- 55 Antibodies elicited or identified using a FmoPV described herein may be used in diagnostic immunoassays, passive

immunotherapy, and generation of antiidiotypic antibodies. The antibodies before being used in passive immunotherapy may be modified, e.g., the antibodies may be chimerized or humanized. See, e.g., U.S. Pat. Nos. 4,444,887 and 4,716,111; and International Publication Nos. WO 98/46645, WO 98/50433, WO 98/24893, WO 98/16654, WO 96/34096, WO 96/33735, and WO 91/10741, each of which is incorporated herein by reference in its entirety, for reviews on the generation of chimeric and humanized antibodies. In addition, the ability of the antibodies to neutralize FmoPV and the specificity of the antibodies for FmoPV antigens may be tested prior to using the antibodies in passive immunotherapy. Antibodies against FmoPV antigens are used to detect the presence of FmoPV in a subject. In specific embodiments, FmoPV antibodies are used to diagnose FmoPV infections in feline. In specific embodiments, FmoPV antibodies are used to diagnose TIN in feline.

The antibodies elicited or identified using a FmoPV described herein may be incorporated into compositions. In a specific embodiment, the compositions are pharmaceutical compositions. In some embodiments, a pharmaceutical composition may comprise one or more other therapies in addition to an antibody. The pharmaceutical compositions provided herein can be in any form that allows for the composition to be administered to a subject. In a specific embodiment, the pharmaceutical compositions are suitable for veterinary and/or human administration. In another specific embodiment, the antibody compositions are formulated for the intended route of administration (e.g., parenteral, intranasal, or pulmonary administration). The antibody compositions may be used in methods of preventing and/or treating a FmoPV infection. The antibody compositions may also be used in methods or preventing and/or treating FmoPV disease.

Antibodies elicited or identified using a FmoPV described herein may be used to monitor the efficacy of a therapy and/or disease progression. Any immunoassay system known in the art may be used for this purpose including, but not limited to, competitive and noncompetitive assay systems using techniques such as radioimmunoassays, ELISA (enzyme linked immunosorbent assays), "sandwich" immunoassays, precipitin reactions, gel diffusion precipitin reactions, immunodiffusion assays, agglutination assays, complement fixation assays, immunoradiometric assays, fluorescent immunoassays, protein A immunoassays and immunoelectrophoresis assays, to name but a few.

5.8 Prophylactic & Therapeutic Uses

In one aspect, provided herein are methods for inducing an immune response in a subject utilizing a FmoPV described herein or an immunogenic composition thereof. In a specific embodiment, a method for inducing an immune response to a FmoPV in a subject comprises administering to a subject in need thereof an effective amount of a FmoPV or an immunogenic composition thereof. In certain embodiments, the FmoPV or immunogenic composition thereof expresses FmoPV proteins from two or more types, subtypes or strains of FmoPV, and thus, may be used to induce an immune response to two or more types, subtypes or strains of FmoPV. In a specific embodiment, a method for inducing an immune response to a FmoPV in a subject comprises administering to a subject in need thereof a FmoPV described herein as a live virus vaccine. In particular embodiments, the live virus vaccine comprises an attenuated virus. In another embodiment, a method for inducing an immune response to FmoPV in a

subject comprises administering to a subject in need thereof a FmoPV described herein as an inactivated virus vaccine.

In another aspect, provided herein are methods for preventing and/or treating a FmoPV infection in a subject utilizing a FmoPV described herein or a pharmaceutical composition thereof. In one embodiment, a method for preventing or treating a FmoPV infection in a subject comprises administering to a subject in need thereof an effective amount of a FmoPV or a composition thereof. In another embodiment, a method for preventing or treating an FmoPV infection in a subject comprises administering to a subject in need thereof an effective amount of a FmoPV or a pharmaceutical composition thereof and one or more other therapies. In another embodiment, a method for preventing or treating a FmoPV infection in a subject comprises administering to a subject in need thereof a FmoPV described herein as a live virus vaccine. In particular embodiments, the live virus vaccine comprises an attenuated virus. In another embodiment, a method for preventing or treating a FmoPV infection in a subject comprises administering to a subject in need thereof a FmoPV described herein as an inactivated virus vaccine.

In another aspect, provided herein are methods for preventing and/or treating a FmoPV in a subject utilizing a FmoPV described herein or a pharmaceutical composition thereof. In a specific embodiment, a method for preventing or treating a FmoPV disease in a subject comprises administering to a subject in need thereof an effective amount of a FmoPV or a pharmaceutical composition thereof. In another embodiment, a method for preventing or treating a FmoPV in a subject comprises administering to a subject in need thereof an effective amount of a FmoPV or a pharmaceutical composition thereof and one or more other therapies. In another embodiment, a method for preventing or treating a FmoPV disease in a subject comprises administering to a subject in need thereof a FmoPV described herein as a live virus vaccine. In particular embodiments, the live virus vaccine comprises an attenuated virus. In another embodiment, a method for preventing or treating a FmoPV disease in a subject comprises administering to a subject in need thereof a FmoPV described herein as an inactivated virus vaccine.

5.9 Dosage and Frequency of Administration

A FmoPV, an antibody or a composition described herein may be delivered to a subject by a variety of routes. These include, but are not limited to, intranasal, intratracheal, oral, intradermal, intramuscular, topical intraperitoneal, transdermal, intravenous, pulmonary, conjunctival and subcutaneous routes. In some embodiments, a composition is formulated for topical administration, for example, for application to the skin. In specific embodiments, the composition is formulated for nasal administration, e.g., as part of a nasal spray. In certain embodiments, a composition is formulated for intramuscular administration. In some embodiments, a composition is formulated for subcutaneous administration. In specific embodiments for live virus vaccines, the vaccine is formulated for administration by a route other than injection. In some embodiments it may be desirable to introduce the pharmaceutical compositions into the lungs by any suitable route. Pulmonary administration can also be employed, e.g., by use of an inhaler or nebulizer, and formulation with an aerosolizing agent for use as a spray.

In some embodiments, when a FmoPV or a composition thereof is administered to a non-human subject (e.g., a cat), the virus or composition is administered orally to the subject in the subject's food. In other embodiments, when a FmoPV or a composition thereof is administered to a subject (e.g.,

cat), the virus or composition is administered orally to the subject in the subject's water. In other embodiments, when a FmoPV or a composition thereof is administered to a non-human subject, the virus or composition is administered by spraying the subject with the virus or composition.

The amount of a FmoPV, an antibody or composition described herein which will be effective in the treatment and/or prevention of a FmoPV infection or a FmoPV disease will depend on the nature of the disease, and can be determined by standard techniques. The precise dose to be employed in the formulation will also depend on the route of administration, and the seriousness of the infection or disease caused by it, and should be decided according to the judgment of the practitioner and each subject's circumstances. For example, effective doses may also vary depending upon means of administration, target site, physiological state of the subject (including age, body weight, health), whether the subject is human or an animal, whether other medications are administered, and whether treatment is prophylactic or therapeutic. Similarly, the amount of a FmoPV or a composition thereof that will be effective as a delivery vector will vary and can be determined by standard techniques. Treatment dosages are optimally titrated to optimize safety and efficacy.

In certain embodiments, an *in vitro* assay is employed to help identify optimal dosage ranges. Effective doses may be extrapolated from dose response curves derived from *in vitro* or animal model test systems.

Exemplary doses for live FmoPV may vary from 10-100, or more, virions per dose. In some embodiments, suitable dosages of a live FmoPV virus are 10^2 , 5×10^2 , 10^3 , 5×10^3 , 10^4 , 5×10^4 , 10^5 , 5×10^5 , 10^6 , 5×10^6 , 10^7 , 5×10^7 , 10^8 , 5×10^8 , 1×10^9 , 5×10^9 , 1×10^{10} , 5×10^{10} , 1×10^{11} , 5×10^{11} or 10^{12} pfu, and can be administered to a subject once, twice, three or more times with intervals as often as needed. In another embodiment, a live FmoPV is formulated such that a 0.2-mL dose contains $10^{6.5}$ - $10^{7.5}$ fluorescent focal units of live FmoPV. In another embodiment, an inactivated vaccine is formulated such that it contains about 15 µg to about 100 µg, about 15 µg to about 75 µg, about 15 µg to about 50 µg, or about 15 µg to about 30 µg of a FmoPV protein.

In certain embodiments, a FmoPV described herein or a composition thereof is administered to a subject as a single dose followed by a second dose 3 to 6 weeks later. In accordance with these embodiments, booster inoculations may be administered to the subject at 6 to 12 month intervals following the second inoculation. In certain embodiments, the booster inoculations may utilize a different FmoPV strain or a composition thereof. In some embodiments, the administration of the same FmoPV strain or a composition thereof may be repeated and the administrations may be separated by at least 1 day, 2 days, 3 days, 5 days, 10 days, 15 days, 30 days, 45 days, 2 months, 75 days, 3 months, or at least 6 months.

For passive immunization with an antibody, the dosage ranges from about 0.0001 to 100 mg/kg, and more usually 0.01 to 50 mg/kg or 0.1 to 15 mg/kg, of the subject body weight. For example, dosages can be 1 mg/kg body weight or 10 mg/kg body weight or within the range of 1-10 mg/kg or in other words, 70 mg or 700 mg or within the range of 70-700 mg, respectively, for a 70 kg patient. An exemplary treatment regime entails administration once per every two weeks or once a month or once every 3 to 6 months for a period of one year or over several years, or over several year-intervals. In some methods, two or more monoclonal antibodies with different binding specificities are administered simultaneously, in which case the dosage of each antibody administered falls within the ranges indicated. Antibody is usually administered on multiple occasions. Intervals between single dosages can

be weekly, monthly or yearly. Intervals can also be irregular as indicated by measuring blood levels of antibody to the FmoPV in the patient.

5.10 Screening Assays

In one aspect, a FmoPV described herein may be used to study the life cycle of a FmoPV. For example, a FmoPV described herein that expresses a detectable heterologous sequence (e.g., a detectable substance such as described above) is introduced into a host cell and the life cycle of the virus is monitored by the assessing the expression of the detectable heterologous sequence. A FmoPV described herein that expresses a detectable heterologous sequence may also be administered to a non-human animal and the infection monitored by assessing the expression of the detectable heterologous sequence.

In another aspect, provided herein are high throughput screening assays for the identification or validation of compounds that modulate the replication of negative-sense, single-stranded RNA viruses, in particular FmoPV. In a specific embodiment, the high throughput screening assay to identify a compound that modulates the replication of a negative-sense, single-stranded RNA virus (in particular FmoPV) comprises: (a) contacting a compound or a member of a library of compounds with a host cell infected with a FmoPV described herein that expresses a detectable heterologous nucleotide sequence; and (b) measuring the expression or activity of a product encoded by the detectable heterologous nucleotide sequence. In another embodiment, the high throughput screening assay to identify a compound that modulates the replication of a negative-sense, single-stranded RNA virus (in particular FmoPV) comprises: (a) infecting a host cell with a FmoPV described herein that expresses a detectable heterologous nucleotide sequence in the presence of a compound or a member of a library of compounds; and (b) measuring the expression or activity a product encoded by the detectable heterologous nucleotide sequence. In another embodiment, the high throughput screening assay to identify a compound that modulates the replication of a negative-sense, single-stranded RNA virus (in particular FmoPV) comprises: (a) contacting a host cell with a compound or a member of a library of compounds; (b) infecting the host cell with a FmoPV described herein that expresses a detectable heterologous nucleotide sequence; and (c) measuring the expression or activity a product encoded by the detectable heterologous nucleotide sequence.

Any method known to one of skill in the art can be used to measure the expression or activity of a product encoded by the detectable heterologous nucleotide sequence. In one embodiment, the product encoded by the detectable heterologous nucleotide sequence is RNA and a technique known to one of skill in the art, such as RT-PCR or Northern blot analysis, is used to measure the expression of the RNA product. In another embodiment, the product encoded by the detectable heterologous nucleotide sequence is protein and a technique known to one of skill in the art, such as western blot analysis or an ELISA, is used to measure the expression of the protein product. In another embodiment, the product encoded by the detectable heterologous nucleotide sequence is protein and the activity of the protein is measured using a technique known to one of skill in the art.

Any screening assay described herein can be performed individually, e.g., just with the test compound, or with appropriate controls. For example, a parallel assay without the test compound, or other parallel assays without other reaction components (e.g., virus) can be performed. In one embodiment,

ment, a parallel screening assay as described above is performed except that a negative control and/or a positive control are used in place of a test compound. In another embodiment, to eliminate cytotoxic compounds that appear as false positives, a counter screen is performed in which uninfected cells are transfected with a nucleic acid construct (e.g., a plasmid) comprising a detectable heterologous nucleotide sequence and the expression or activity of a product encoded by the detectable heterologous nucleotide sequence is measured. Alternatively, it is possible to compare assay results to a reference, e.g., a reference value, e.g., obtained from the literature, a prior assay, and so forth. Appropriate correlations and art known statistical methods can be used to evaluate an assay result.

In another aspect, the antiviral effect of a compound on FmoPV can be assessed in a non-human animal using a FmoPV described herein. In one embodiment, the antiviral effect of a compound on FmoPV can be assessed by a method comprising: (a) administering (for example, parenterally, subcutaneously, intranasally, or intraperitoneally) to a non-human subject, concurrently, subsequently or prior to administration of a compound, an effective amount of a FmoPV described herein; b) waiting for a time interval following the administration of the FmoPV; and d) detecting the FmoPV in the subject or in a biological specimen from the subject.

5.11 Kits

In one aspect, provided herein is a kit comprising, in one or more containers, one or more nucleic acid sequences described herein. In a specific embodiment, a kit comprises, in a container, a FmoPV gene segment or a complement thereof. In another embodiment, a kit comprises, in one, two or more containers, a nucleic acid sequence encoding a FmoPV gene segments or a complement thereof. The kit may further comprise one or more of the following: host cells suitable for rescue of the virus, reagents suitable for transfecting plasmid DNA into a host cell, helper virus, plasmids encoding one or more types of FmoPV gene segments, one or more expression plasmids encoding viral proteins, and/or one or more primers specific for a FmoPV gene segment or a complement thereof, or nucleic acid sequences encoding the same.

In another aspect, provided herein is a kit comprising one or more containers filled with one or more of the one or more FmoPV described herein or a composition thereof. In a specific embodiment, provided herein is a pharmaceutical pack or kit comprising, in one or more containers, a composition comprising one or more FmoPV described herein. In another aspect, provided herein is a kit comprising, in one or more containers, primers specific for a particular FmoPV gene segment.

In another aspect, provided herein is a kit comprising one or more containers filled with one or more antibodies generated or identified using a FmoPV described herein. In one embodiment, a kit comprises an antibody described herein, preferably an isolated antibody, in one or more containers. In a specific embodiment, a kit encompassed herein contains an isolated FmoPV antigen that the antibodies encompassed herein react with as a control. In a specific, a kit provided herein further comprise a control antibody which does not react with a FmoPV antigen that an antibody encompassed herein reacts with. In another specific embodiment, a kit provided herein contains a means for detecting the binding of an antibody to a FmoPV antigen that an antibody encompassed herein reacts with (e.g., the antibody may be conjugated to a detectable substrate such as a fluorescent com-

pound, an enzymatic substrate, a radioactive compound or a luminescent compound, or a second antibody which recognizes the first antibody may be conjugated to a detectable substrate). In specific embodiments, a kit may include a recombinantly produced or chemically synthesized FmoPV antigen. The FmoPV antigen provided in the kit may also be attached to a solid support. In a more specific embodiment the detecting means of the above described kit includes a solid support to which a FmoPV antigen is attached. Such a kit may also include a non-attached reporter-labeled anti-human antibody. In this embodiment, binding of the antibody to the FmoPV antigen can be detected by binding of the said reporter-labeled antibody.

Optionally associated with such a kit can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration.

Example 2 demonstrates a diagnostic test done by RT-PCR. Another diagnostic test, demonstrated in Example 3, is a viral load test using real-time quantitative RT-PCR using the above genomic information obtained from sequencing.

5.12 Complete Genome Sequencing and Analysis

Three complete genomes of FmoPV, from two urine (761U, 776U) and one rectal swab (M252A) samples, were amplified and sequenced using RNA extracted directly from the specimens as templates with a strategy described in our previous publications (13, 14). Genome analysis was performed as described in our previous publications (13, 14, 23, 24, 25). Phylogenetic trees were constructed by maximum likelihood method using PhyML 3.0 (26).

The complete genome sequences of three strains of FmoPV designated 761U, 776U and M252A were determined. The genome sequence for FmoPV strain 761U was deposited at GenBank and given accession number JQ411014. The FmoPV 761U nucleotide sequence is shown in FIG. 2. The genome sequence for FmoPV strain 776U was deposited at GenBank and given accession number JQ411015. The FmoPV 776U nucleotide sequence is shown in FIG. 3. The genome sequence for FmoPV strain M252A was deposited at GenBank and given accession number JQ411016. The FmoPV M252A nucleotide sequence is shown in FIG. 4.

The genome size of these FmoPV nucleotide sequences are 16050 bases and G+C contents 35.1% to 35.3%, with FmoPV having the largest genome among all *morbilliviruses* with genome sequences available (see FIG. 1). The genome of FmoPV conforms to the rule of six as in other *paramyxovirus* genomes. It contains a 12-nt complementary 3' leader and 5' trailer sequence. The 3' leader sequence is 55 nt. In contrast to other *morbilliviruses* which only have 5' trailer sequences of 40 or 41 nt, the genome of FmoPV has a trailer sequence of 400 nt, accounting for its bigger genome size. Such long trailer sequences of >400 nt have only been observed in avian *paramyxoviruses* 3 (681-707 nt) and 5 (552 nt) and tupaia *paramyxovirus* (590 nt).

Similar to other *morbilliviruses*, the genome of FmoPV contains six genes (3'-N-P/V/C-M-F-H-L-5') (see FIG. 1). Pairwise alignment of the predicted gene products among FmoPV and other *paramyxoviruses* showed the highest amino acid identities with members of the genus *Morbillivirus*, with the N, P/V/C(P), P/V/C(V), P/V/C(C), M, F, H and L of FmoPV having 54.3-56.8%, 25.6-31.7%, 20.7-25.7%, 18.3-25.4%, 57.6-60.0%, 35.8-45.1%, 20.4-24.1% and 55.2-57.3% amino acid identities to those of other *morbilliviruses* (see Table 1). The lengths and characteristics of the major structural genes and intergenic regions (IGRs) are summarized in Table 2.

TABLE 1

Pairwise amino acid identities of predicted gene products of FmoPV compared to other paramyxoviruses									
Paramyxoviruses	Percentage of amino acid sequence identity								
	N			P			M		
	761U	776U	M252A	761U	776U	M252A	761U	776U	M252A
Morbillivirus									
FmoPV 761U	—	99.2	96.0	—	97.4	89.2	—	98.8	95.8
FmoPV 776U	99.2	—	96.1	97.4	—	88.6	98.8	—	96.4
FmoPV M252A	96.0	96.1	—	89.2	88.6	—	95.8	96.4	—
CdiPV	56.8	56.5	56.2	29.7	29.3	27.5	58.8	58.5	58.8
DmoPV	54.5	54.3	55.0	26.4	25.8	25.6	59.3	59.6	59.5
MeaPV	55.4	55.2	54.6	29.0	28.8	27.8	60.0	59.7	59.0
PprPV	55.6	55.8	55.8	31.6	31.7	31.6	58.2	58.5	58.8
RinPV	55.5	55.5	55.6	28.4	28.4	26.8	59.5	59.2	58.2
PdiPV	56.6	56.2	56.2	30.6	30.4	28.8	57.9	57.9	57.6
Avulavirus									
AviPV-6	29.1	29.3	28.1	18.3	17.9	18.6	23.5	23.5	22.9
NdiPV	27.1	27.1	28.0	19.8	18.8	18.1	19.5	20.0	20.9
Henipavirus									
HenPV	33.6	33.2	32.8	21.1	22.2	23.3	43.9	44.2	44.2
NipPV	33.8	33.4	33.0	22.4	21.8	22.8	43.1	43.3	43.4
Respirovirus									
BpiPV-3	25.7	25.9	25.4	18.0	18.7	19.2	33.9	33.6	34.2
SenPV	24.2	25.2	25.0	19.0	18.5	20.5	34.7	34.7	34.4
Rubulavirus									
HpiPV-2	27.5	27.7	27.9	19.4	19.6	16.8	22.8	23.1	21.8
MumPV	27.6	27.8	27.7	19.6	19.9	17.2	20.4	20.0	20.7
Unclassified Paramyxovirinae									
AsaPV	29.8	29.8	28.4	16.4	17.2	17.1	34.7	34.7	34.7
TlmPV	35.7	36.4	36.0	22.7	22.7	23.0	48.0	48.3	48.8
BeiPV	36.6	36.2	36.3	23.5	23.3	23.9	47.4	47.7	48.5
FdlPV	28.4	28.4	28.5	19.9	21.1	20.8	34.9	34.5	33.9
JPV	34.0	34.0	34.0	23.1	23.3	22.3	47.8	48.1	48.4
MosPV	38.6	38.6	37.6	22.9	22.9	22.0	47.5	48.2	46.9
TupPV	33.4	32.7	32.1	23.2	23.2	23.9	43.9	43.2	42.5
NarPV	37.2	36.9	38.1	22.7	23.8	22.6	51.5	51.5	50.6
Percentage of amino acid sequence identity									
Paramyxoviruses	F			A			L		
	761U	776U	M252A	761U	776U	M252A	761U	776U	M252A
	Morbillivirus								
FmoPV 761U	—	98.9	96.3	—	99.0	96.3	—	99.4	97.0
FmoPV 776U	98.9	—	95.9	99.0	—	95.3	99.4	—	97.3
FmoPV M252A	96.3	95.9	—	96.3	95.3	—	97.0	97.3	—
CdiPV	36.0	35.8	36.1	20.4	20.6	20.6	55.5	55.4	55.4
DmoPV	43.0	42.2	42.4	24.1	24.1	23.9	56.4	56.4	56.5
MeaPV	44.0	44.0	43.9	20.7	20.9	20.7	56.0	55.9	55.8
PprPV	42.8	42.8	43.2	21.6	21.8	21.6	57.3	57.3	57.2
RinPV	44.6	44.3	45.1	21	21.1	22.4	55.4	55.3	55.2
PdiPV	42.7	42.9	42.9	20.6	20.8	20.9	55.4	55.4	55.7
Avulavirus									
AviPV-6	26.8	27.0	26.6	17.7	17.6	17.3	28.5	28.6	29.1
NdiPV	25.8	25.8	25.4	17.5	17.2	16.2	27.7	27.5	27.6
Henipavirus									
HenPV	32.4	32.6	33.0	17.8	17.8	18.9	43.4	43.4	43.4
NipPV	33.0	33.2	33.3	18.2	18.2	18.9	44.9	44.8	45.2
Respirovirus									
BpiPV-3	28.5	28.2	28.5	18.9	18.9	18.2	38.4	38.6	38.9
SenPV	27.1	26.5	26.5	20.5	20.3	21.1	39.1	39.3	39.4

TABLE 1-continued

Pairwise amino acid identities of predicted gene products of FmoPV compared to other paramyxoviruses										
Rubulavirus										
HpiPV-2	25.0	24.4	25.0	18.0	18.0	18.3	30.4	30.2	30.2	
MumPV	26.4	26.2	25.7	18.1	17.8	18.7	30.0	30.1	29.9	
Unclassified										
Paramyxovirinae										
AsaPV	30.9	30.6	30.8	20.1	20.1	19.0	40.0	40.1	40.4	
TlmPV	32.7	32.9	33.0	16.1	15.8	16.6	46.4	46.4	46.4	
BeiPV	32.9	32.7	32.7	16.1	15.8	15.8	46.3	46.3	46.6	
FdIPV	29.0	29.2	29.7	19.9	19.9	19.2	40.0	40.0	39.7	
JPV	31.8	31.8	32.9	14.8	15.0	14.4	46.9	46.9	47.2	
MosPV	36.3	36.3	35.8	19.0	19.2	19.9	48.6	48.8	48.8	
TupPV	35.0	35.4	35.0	14.7	14.4	15.6	47.3	47.2	47.1	
NarPV	33.0	32.5	32.6	18.6	18.4	18.7	47.7	48.0	47.9	

TABLE 2

Molecular features and predicted gene products of FmoPV and other morbilliviruses											
Virus	Gene	mRNA features (nt)					Deduced protein				
		Total length	5' UTR	ORF	3' UTR	hexamer phase	Intergenic regions (nt)	Size (aa)	MW (kDa)	pI	Coding frame
FmoPV	Leader	55					(TTT)				
761U	N	1659	52	1560	47	2	CTT	519	57.01	5.27	3
	P/V/C(P)	1637	63	1476	98	2	CTT	491	53.12	5.20	2
	P/V/C(V)	1638	63	831	744	2	CTT	276	29.97	4.85	2
	P/V/C(C)	1637	94	513	1030	2	CTT	170	19.90	9.69	3
	M	1378	31	1014	333	4	CTA	337	38.05	9.29	2
	F	2191	215	1632	344	5	CTT	543	60.26	8.80	1
	H	1934	30	1788	116	3	CTT	595	68.11	6.25	3
	L	6781	22	6609	150	2	(CTT)	2202	252.87	8.32	3
	Trailer	400									
FmoPV	Leader	55					(TTT)				
776U	N	1659	52	1560	47	2	CTT	519	57.06	5.15	3
	P/V/C(P)	1637	63	1476	98	2	CTT	491	53.19	5.33	2
	P/V/C(V)	1638	63	831	744	2	CTT	276	29.99	4.91	2
	P/V/C(C)	1637	94	513	1030	2	CTT	170	19.87	9.69	3
	M	1378	31	1014	333	4	CTA	337	38.02	9.29	2
	F	2191	215	1632	344	5	CTT	543	60.21	8.79	1
	H	1934	30	1788	116	3	CTT	595	68.24	6.03	3
	L	6781	22	6609	150	2	(CTT)	2202	253.01	8.23	3
	Trailer	400									
FmoPV	Leader	55					(TTT)				
M252A	N	1659	52	1560	47	2	CTT	519	57.08	5.34	3
	P/V/C(P)	1637	63	1476	98	2	CTT	491	53.41	5.44	2
	P/V/C(V)	1638	63	831	744	2	CTT	276	29.94	5.13	2
	P/V/C(C)	1637	94	513	1030	2	CTT	170	19.86	9.69	3
	M	1378	31	1014	333	4	CTA	337	38.06	9.29	2
	F	2191	215	1632	344	5	CTT	543	60.19	8.80	1
	H	1934	30	1788	116	3	CTT	595	68.18	6.25	3
	L	6781	22	6609	150	2	(CTT)	2202	252.91	8.28	3
	Trailer	400									
MeaPV	Leader	55					(CTT)				
	N	1689	52	1578	59	2	CTT	525	58.02	5.11	3
	P/V/C(P)	1655	59	1524	72	2	CTT	507	53.90	4.99	1
	P/V/C(V)	1656	59	900	697	2	CTT	299	31.85	4.66	1
	P/V/C(C)	1655	81	561	1013	2	CTT	186	21.11	10.36	2
	M	1466	32	1008	426	4	CTT	335	37.71	9.07	3
	F	2373	583	1653	137	3	CTT	550	59.53	8.78	1
	H	1958	20	1854	84	3	CGT	617	69.17	7.88	2
	L	6643	22	6552	69	2	(CTT)	2183	247.74	8.43	3
	Trailer	40									
CdiPV	Leader	55					(CTT)				
	N	1683	52	1572	59	2	CTT	523	58.14	5.20	3
	P/V/C(P)	1655	59	1524	72	2	CTT	507	54.75	5.03	1
	P/V/C(V)	1656	59	900	697	2	CTT	299	33.11	4.66	1
	P/V/C(C)	1655	81	525	1049	2	CTT	174	20.26	10.30	2
	M	1447	32	1008	407	4	CTT	335	37.77	8.87	3
	F	2206	85	1989	132	2	CTT	662	72.95	9.18	3
	H	1946	20	1815	111	3	CTA	604	67.99	6.74	2

TABLE 2-continued

Molecular features and predicted gene products of FmoPV and other morbilliviruses												
Virus	Gene	mRNA features (nt)						Deduced protein				
		Total length	5' UTR	ORF	3' UTR	hexamer phase	Intergenic regions (nt)	Size (aa)	MW (kDa)	pI	Coding frame	
DmoPV	L	6642	22	6555	65	2	(CAA)	2184	248.19	8.39	3	
	Trailer	41										
	Leader	55					(CTT)					
	N	1683	52	1572	59	2	CTT	523	57.49	5.14	3	
	P/V/C(P)	1655	59	1521	75	2	CTT	506	55.26	5.09	1	
	P/V/C(V)	1656	59	912	685	2	CTT	303	33.69	4.75	1	
	P/V/C(C)	1655	81	534	1040	2	CTT	177	20.41	10.19	2	
	M	1453	32	1008	413	4	CTT	335	37.97	8.97	3	
	F	2212	421	1659	132	2	CTT	552	59.87	8.81	3	
	H	1946	20	1815	111	3	CTT	604	68.04	6.18	2	
PprPV	L	6643	22	6552	69	2	(CAA)	2183	248.07	8.52	3	
	Trailer	40										
	Leader	55					(CTT)					
	N	1689	52	1578	59	2	CTT	525	57.78	5.21	3	
	P/V/C(P)	1655	59	1530	66	2	CTT	509	54.79	5.14	1	
	P/V/C(V)	1656	59	897	700	2	CTT	298	31.34	4.58	1	
	P/V/C(C)	1655	81	534	1040	2	CTT	177	19.93	9.92	2	
	M	1483	32	1008	443	4	CTT	335	37.95	8.97	3	
	F	2411	634	1641	136	2	CTT	546	59.12	8.71	3	
	H	1957	20	1830	107	4	CTT	609	68.76	6.64	3	
RinPV	L	6643	22	6552	69	2	(CTA)	2183	247.27	7.73	3	
	Trailer	40										
	Leader	55					(CTT)					
	N	1689	52	1578	59	2	CTT	525	58.04	5.08	3	
	P/V/C(P)	1655	59	1524	72	2	CTT	507	54.36	4.82	1	
	P/V/C(V)	1656	59	900	697	2	CTT	299	32.57	4.56	1	
	P/V/C(C)	1655	81	534	1040	2	CTT	177	19.93	10.29	2	
	M	1460	32	1008	420	4	CTT	335	37.54	9.15	3	
	F	2367	589	1641	137	3	CTT	546	58.73	8.43	1	
	H	1958	20	1830	108	3	CGT	609	67.90	6.61	2	
55	L	6643	22	6552	69	2	(CTT)	2183	248.21	8.48	3	
	Trailer	40										

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The conserved N-terminal motif MA(T/S)L in *morbilliviruses* was absent in the N protein of FmoPV, which contained the sequence MSSL (SEQ ID NO: 13) as a result of A→S (G→U at first codon position) substitution at the second amino acid (FIG. 5). Similar to the nuclear localization signal (NLS) of the N proteins in CdiPV, MeaPV and RinPV but different from the classical NLS sequence (PMID: 16716375), a leucine/isoleucine-rich motif at amino acid positions 70-77 is identified in the N protein of FmoPV (see SI FIG. 5). Similar to the nuclear export signal (NES) of the N proteins in CdiPV and RinPV, a leucine-rich motif at amino acid positions 4-11 is also identified in the N protein of FmoPV (see FIG. 5).

As in other *morbilliviruses*, the P/V/C gene of FmoPV contains two initiation codons, the first one for translation of P and V and the second for translation of C. Similar to most members of Paramyxoviridae, the P/V/C gene of FmoPV contains a UC-rich editing site that allows the addition of non-templated G residues to mRNA products during P/V/C gene transcription, resulting in the production of different proteins with a common N-terminal region. In all three strains of FmoPV, this common N-terminal region consists of 226 amino acids.

To determine the exact location of P gene editing site and the number and frequency of G-residue insertions, a small cDNA fragment including the UC-rich region was amplified, cloned and sequenced using mRNA extracted from FmoPV infected CRFK cells. Among 23 independent clones sequenced, 13 contained the sequence TTAAAGGGGG (without G insertion, encoding P protein) and 10 contained the sequence TTAAAAGGGGG (one G inserted, encoding V

protein). The sequence TTA_nG_n is conserved as in other *paramyxovirus* editing sites except for those of *rubulaviruses*. In contrast to other *morbilliviruses* in which the sequence is TTA₅G₃ (SEQ ID NO: 16) (33), the TTA_nG_n sequence in FmoPV is TTA₄G₄ (SEQ ID NO: 14).

Different from all other known *morbilliviruses*, the F protein of FmoPV has a single-basic protein cleavage site, whereas the cleavage sites in other *morbilliviruses* are multi-basic (34). Cellular trypsin-like protease cleaves the F protein into F1 and F2 before cell fusion occurs, which facilitates the isolation of these viruses in cell lines. Two heptad repeat sequences similar to those in F proteins of other *paramyxoviruses* were also identified in the F₁ of FmoPV. The F protein of FmoPV also contains the 10 Cys residues that are highly conserved in other *morbilliviruses* and 5 potential N-glycosylation sites, most of which located in the F₂ peptide.

Phylogenetic trees constructed using the predicted amino acid sequences of N, P, M, F, H and L genes of FmoPV and other members of Paramyxoviridae are shown in FIG. 7. In all six trees, the three viruses were clustered with *morbilliviruses*, with high bootstrap supports, forming a distinct subgroup (see FIG. 7). The trees were constructed by maximum likelihood method with bootstrap values calculated from 1000 trees and rooted on midpoint. The scale bars in FIG. 7 indicate the branch length that corresponds to 0.5 substitutions per site. Three strains from FmoPV were named as 761U, 776U, M252A. Names and accession numbers of the other viruses in FIG. 7 are listed in Table 3 below.

TABLE 3

Viruses and GenBank accession numbers		
Abbreviation	Virus name	GenBank accession no.
AsaPV	Atlantic Salmon paramyxovirus	EU156171
AviPV-5	Avian paramyxovirus 5	GU206351
AviPV-6	Avian paramyxovirus 6	NC_003043
AviPV-7	Avian paramyxovirus 7	FJ231524
BeiPV	Beilong virus	NC_007803
BpiPV-3	Bovine parainfluenza virus 3	NC_002161
CdiPV	Canine distemper virus	NC_001921
DmoPV	Dolphin morbillivirus	NC_005283
FdlPV	Fer-de-lance virus	NC_005084
GooPV	Goose paramyxovirus SF02	NC_005036
HenPV	Hendra virus	NC_001906
HpiPV-1	Human parainfluenza virus 1	NC_003461
HpiPV-2	Human parainfluenza virus 2	NC_003443
HpiPV-3	Human parainfluenza virus 3	NC_001796
HpiPV-4a	Human parainfluenza virus 4a	BAJ11741
HuRSV	Human respiratory syncytial virus	NC_001781
JPV	J-virus	NC_007454
MeaPV	Measles virus	NC_001498
MosPV	Mossman virus	NC_005339
MumPV	Mumps virus	NC_002200
NarPV	Nariva virus	FJ362497
NdiPV	Newcastle disease virus	NC_002617
NipPV	Nipah virus	NC_002728
PdiPV	Phocine distemper virus	P35944, P35939, BAA01205, BAA01206, CAA12080, CAA70843

TABLE 3-continued

Viruses and GenBank accession numbers			
	Abbreviation	Virus name	GenBank accession no.
5	PprPV	Peste-des-petits-ruminants virus	NC_006383
	RinPV	Rinderpest virus	NC_006396
	SenPV	Sendai virus	NC_001552
10	SpiPV-3	Swine para influenza virus 3	EU439429
	ThkPV-1	Tuhoko virus 1	GU128080
	ThkPV-2	Tuhoko virus 2	GU128081
	ThkPV-3	Tuhoko virus 3	GU128082
	TlmPV	Tailam virus	JN689227
15	TupPV	Tupaia paramyxovirus	NC_002199

5.13 Detection of FmoPV Infection in Felines

20 Infection of a feline by FmoPV can be detected in sera by
the use of immunofluorescent antibodies as demonstrated in
Example 9, or by the detection of neutralizing antibodies as
demonstrated in Example 10. Of the 27 cat sera samples
25 tested in Example 9, immunofluorescent antibody was
detected from 7 cats with titer from 1:40 to 1:640. Table 4
below shows the association between TIN and evidence of
FmoPV infection.

TABLE 4

The same 27 cat sera samples used in Example 9 were tested for the presence of neutralization antibody in Example 10. Neutralization antibody was detected from 6 cats with titer from 1:20 to 1:40, shown below in Table 5, of which all are positive for immunofluorescent antibody (Table 4).

species specificity in FmoPV. Although no recombination was identified in the present FmoPV strains (data not shown), other viruses from cats, such as feline *coronaviruses* and feline papillomavirus, have been shown to be closely related to or recombine with their canine counterparts in dogs, sug-

TABLE 5

Sample No.	Neutralizing antibody detected from cats' sera								
	1:10	1:20	1:40	1:80	1:160	1:320	1:640	1:1280	1:2560
1357	+	+	-	-	-	-	-	-	-
1359	+	+	-	-	-	-	-	-	-
1363	-	-	-	-	-	-	-	-	-
1364	-	-	-	-	-	-	-	-	-
1365	-	-	-	-	-	-	-	-	-
1366	-	-	-	-	-	-	-	-	-
1367	-	-	-	-	-	-	-	-	-
1368	-	-	-	-	-	-	-	-	-
1391	-	-	-	-	-	-	-	-	-
1392	+	+	-	-	-	-	-	-	-
1393	+	+	-	-	-	-	-	-	-
1394	-	-	-	-	-	-	-	-	-
1395	-	-	-	-	-	-	-	-	-
1396	-	-	-	-	-	-	-	-	-
1397	-	-	-	-	-	-	-	-	-
1402	-	-	-	-	-	-	-	-	-
1403	-	-	-	-	-	-	-	-	-
1404	-	-	-	-	-	-	-	-	-
1405	-	-	-	-	-	-	-	-	-
1406	-	-	-	-	-	-	-	-	-
1407	+	+	-	-	-	-	-	-	-
1408	-	-	-	-	-	-	-	-	-
1409	+	+	+	-	-	-	-	-	-
1417	-	-	-	-	-	-	-	-	-
1418	-	-	-	-	-	-	-	-	-
1419	-	-	-	-	-	-	-	-	-
1420	-	-	-	-	-	-	-	-	-

6. EXAMPLES

Described herein is a novel feline *paramyxovirus*, FmoPV, from stray cats in Hong Kong, which represents the first documentation of *paramyxoviruses* found in the domestic cat (*Felis catus*). Woo et al. (2012) "Feline morbillivirus, a novel paramyxovirus associated with tubulointerstitial nephritis in domestic cats," PNAS (in press), which is incorporated herein by reference in its entirety.

A molecular epidemiology study was carried out in stray cats in Hong Kong and on diseased cats from mainland China from which the novel feline *paramyxovirus*, FmoPV, was isolated and characterized as shown in the following examples.

To summarize, FmoPV was detected in the urine samples of 53 of 457 stray cats and in the rectal swab and blood samples of four and one of these cats, respectively. Western blot analysis revealed a seroprevalence of 27.8% among tested cats for IgG against recombinant N protein and the presence of antibody is highly associated with the presence of virus. Analysis of the complete genomes of three FmoPV strains, described earlier in Section 5.12, showed that they formed a distinct cluster among the *morbilliviruses* in all six phylogenetic trees constructed using the N, P, M, F, H and L genes (FIG. 7). Immunohistochemistry also showed that, similar to other *morbilliviruses* such as measles virus, FmoPV infects both mononuclear cells and parenchymal cells (FIG. 10). The three strains of FmoPV exhibited high sequence similarity and identical genome organization, suggesting a single species of FmoPV and a high degree of

gesting that feline viruses may have the potential to cross species barrier in animals of similar living habitat (17, 35).

Some recent studies suggested that feline TIN is mediated by an autoimmune mechanism because cats vaccinated with CRFK cell lysates developed antibodies to both CRFK and kidney cell lysates (36-38). Half of these cats sensitized to CRFK lysates on multiple occasions developed tubulointerstitial nephritis at 2 weeks post-sensitization. Sera from CRFK inoculated cats were confirmed to recognize annexin A2 and alpha-enolase by Western blot. In humans, alpha-enolase antibodies are nephritogenic and alpha-enolase and annexin A2 antibodies have been associated with autoimmune diseases. It is therefore possible that a feline nephrotropic virus, such as FmoPV, may trigger off a self-sustained immunopathological process after this acute insult. Notably, some *morbilliviruses*, such as Peste des Petits Ruminants virus, Rinderpest virus and canine distemper virus, have also been found in kidney and/or urine (39-41). Further studies would delineate if these viruses are also associated with renal pathologies in these animals.

Although domestic cats have been associated with humans for almost 10,000 years, they usually pose little physical hazards to humans. However, as a result of cat bites or via other routes, cats can transmit a range of bacteria (e.g. *Bartonella henselae*), protozoa (e.g. *Toxoplasma gondii*), and uncommonly viruses (e.g. rabies virus), causing diseases in humans. Apart from the present novel *paramyxovirus*, viruses of at least 15 families have been found in cats, including the recent discovery of the first picornavirus in cats (23). Moreover, the domestic cats have also been shown to be susceptible

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to infection by highly pathogenic avian influenza viruses H5N1 and H7N7 and SARS *coronavirus*, suggesting that they can be susceptible to viruses associated with serious infections (42-44). A previous survey in Hong Kong showed that one in every eight households was keeping pets with 22.3% keeping cats. The number of locally licensed pet shops selling cats and dogs in Hong Kong has increased from 77 in 2000 to 155 in 2009. In many households, owners having pets share their beds with their pets, and the pet owners often kiss or are being licked by their pets. Such behavior may allow significant exposure to zoonotic agents carried by the pet or parasitizing arthropods (45). Continuous surveillance of viruses in these animals is important to understand their potential for causing emerging infectious diseases in other mammals, including humans.

6.1 Example 1

Sample Collection

The Agriculture Fisheries and Conservation Department (AFCD), Hong Kong provided samples collected from 457 stray cats captured from various locations in Hong Kong over a 2-year period (March 2009 to February 2011) as part of a surveillance program. Tracheal and rectal swabs, urine and blood were collected using procedures described previously (23). In addition, oral and rectal swabs from 16 diseased cats from mainland China were also collected. The study was approved by the Committee on the Use of Live Animals in Teaching and Research, The University of Hong Kong. Samples were collected immediately after euthanasia as routine policies for disposal of locally captured stray cats.

Necropsies of FmoPV-Infected Stray Cats

To identify possible diseases associated with FmoPV, necropsies were performed on two euthanized stray cats positive for FmoPV by RT-PCR. Tissue samples were collected from the lungs; brain; heart; prescapular, retropharyngeal, submandibular and thoracic lymph nodes; spleen; liver; kidneys; urinary bladder; gall bladder; thymus; salivary gland; eyeball; nasal turbinate; intestine; pancreas; foot pads; testicles or ovary; tonsil and adrenal gland. Half of each tissue sample was fixed in 10% neutral buffered formalin for histological processing and the other half was submerged in viral transport medium for RNA extraction and virus isolation.

Since the kidneys of the two stray cats showed histopathological features compatible with TIN, the kidneys, urine and plasma were obtained from a total of 27 strayed cats, including the two cats with necropsies performed, and were subject to RT-PCR, histopathology and antibody detection by western blot and immunofluorescence to examine for possible association between FmoPV infection (RT-PCR and/or antibody positive) and TIN.

6.2 Example 2

RT-PCR of L Gene of *Morbilliviruses* and DNA Sequencing

Viral RNA was extracted from tracheal and rectal swabs, urine and blood using EZ1 Virus Mini Kit (QIAgen) and from tissue samples using QIAamp Viral RNA Mini Kit (QIAgen). *Morbillivirus* detection was performed by amplifying a 155-bp fragment of L gene of *morbilloviruses* using conserved primers (LPW12490 5'-CAGAGACTTAATGAAATT-TATGG-3' (SEQ ID NO: 11) and LPW12491 5'-CCAC-

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CCATCGGGTACTT-3' (SEQ ID NO: 12)) designed by multiple alignments of available L gene sequences of *morbilloviruses*. Reverse transcription, PCR and sequencing were performed according to our previous publications (13, 14).

6.3 Example 3

Real-Time Quantitative RT-PCR

Real-time quantitative RT-PCR to detect L gene of FmoPV was performed on the 56 positive samples using LightCycler FastStart DNA Master SYBR Green I Mix reagent kit (Roche), with primers LPW12490 and LPW12491. Complementary DNA (cDNA) was amplified by LightCycler 2.0 (Roche) with 20- μ l reaction mixtures containing FastStart DNA Master SYBR Green I Mix reagent kit (Roche), 2 μ l of cDNA, 4 mmol/L MgCl₂, and 0.5 mmol/l primers at 95° C. for 10 min, followed by 50 cycles of 95° C. for 10 s, 60° C. for 5 s and 72° C. for 8 s. A plasmid containing the target sequence was used for generating the standard curves.

RT-PCR for a 155-bp fragment in the L gene of *morbilloviruses* was positive in samples from 56 (12.3%) cats from Hong Kong, including 53 urine, 4 rectal swabs and 1 blood specimens. For the 16 diseased cats from mainland China, one (6.25%) cat was RT-PCR positive in both its oral and rectal swabs. Real-time quantitative RT-PCR showed a median viral load of 3.9×10^3 (range 0.037 to 1.4×10^6) copies/ml. Sequencing results suggested the presence of a novel *paramyxovirus* of the genus *Morbillivirus*, with <80% nt identities to known *paramyxoviruses* (FIG. 8). This novel *paramyxovirus* was named FmoPV.

6.4 Example 4

Analysis of P mRNA Editing

To examine the number of G insertions at the P mRNA editing site, mRNA from original specimens was extracted using the Oligotex mRNA Mini kit (QIAgen). First strand cDNA synthesis was performed using SuperScript III kit (Invitrogen) with random hexamer primers. Primers (5'-TTCATCTCTTAGTCCCAGGAA-3' (SEQ ID NO: 17) and 5'-TTTCAGACTCACCTCGATATCT-3' (SEQ ID NO: 18)) were used to amplify a 442-bp product of FmoPV covering the putative editing site. PCR, cloning and sequencing were performed as described in our previous publication (13).

6.5 Example 5

Cloning and Purification of (His)₆-Tagged (“(His)6”

Disclosed as SEQ ID NO: 10 Recombinant Nucleoprotein (N) from *Escherichia coli*

Primers (5'-ACGCGGATCCGATGTCTAGTCTA-3' (SEQ ID NO: 19) and 5'-CGGAATTCCGGTTTTAGAAGGT-CAGTA-3' (SEQ ID NO: 20)) were used to amplify the N gene (519 amino acids) of FmoPV strain 761U by RT-PCR. Cloning, expression and purification of (His)₆-tagged (“(His)6” disclosed as SEQ ID NO: 10) recombinant N protein was performed as described in (1) Lau S K, et al. (2010) Virology 404:106-116; (2) Woo P C, et al. (2005) J Virol 79:884-895; and (3) Woo P C, et al. (2004) Lancet 363:841-845.

6.6 Example 6

Guinea Pig Sera

Guinea pig antiserum against the N protein of FmoPV was produced by injecting 100 μ g purified N protein of FmoPV,

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with an equal volume of complete Freund's adjuvant (Sigma), subcutaneously to three guinea pigs. Incomplete Freund's adjuvant (Sigma) was used in subsequent immunizations. Three inoculations at once every two weeks per guinea pig were administered. Two weeks after the last immunization, 1 ml of blood was taken via the lateral saphenous vein of the guinea pigs to obtain the sera.

Such hyperimmune guinea pig antibody can be used for diagnostic purposes or as a vaccine in the following ways:

1. The recombinant nucleoprotein, N protein, can be used as the target antigen for detecting specific antibody against this virus from cats' sera.
2. The hyperimmune antibody can be used for immunohistochemical detection of viral protein in tissues or infected cell culture to confirm the specific presence of this virus.
3. The recombinant nucleoprotein can be used as a vaccine to induce antibody production.

6.7 Example 7

Western Blot Analysis

Antibodies against the N protein of FmoPV were detected in plasma samples of the 56 cats that were RT-PCR positive and 401 cats that were RT-PCR negative for FmoPV by Western blot. Western blot analysis was performed as described in our previous publications (24, 25, 27), using 1000 ng purified (His)₆-tagged ("(His)6" disclosed as SEQ ID NO: 10) recombinant N protein, 1:1000 dilutions of cat plasma samples, 1:4000 dilution of horse radish peroxidase conjugated goat anti-cat IgG antibody and 1:10000 dilution of goat anti-cat IgM antibody (Bethyl laboratories).

Among tested sera from the 56 cats that were RT-PCR positive and 401 cats that were RT-PCR negative for FmoPV, 49 (76.7%) and 78 (19.4%) were positive for IgG against N protein of FmoPV by western blot analysis respectively ($P<0.0001$) (FIG. 9, Table 6). Among tested sera from the 56 cats that were RT-PCR positive for FmoPV, only 5 (8.9%) were positive for IgM against N protein of FmoPV.

Prominent immunoreactive protein bands of about 69 kDa, consistent with the expected size of 68.7 kDa of the recombinant protein, were detected in three of the six cat serum samples shown in FIG. 9, indicating antigen-antibody interactions between the recombinant FmoPV N protein and serum antibodies. Results of RT-PCR of the corresponding urine samples for FmoPV are also shown.

6.8 Example 8

Viral Culture

Viral culture and electron microscopy were performed according to our previous publications (28, 29). Two hundred microliters of the three samples used for complete genome sequencing were subject to virus culture. After centrifugation, they were diluted five folds with viral transport medium and filtered. 200 μ l of the filtrate was inoculated to 200 μ l of MEM with polybrene. 400 μ l of the mixture was added to 24-well tissue culture plates, with CRFK (feline kidney), B95 (marmoset B-cell), CEF (chicken embryo fibroblast), NIH/3T3 (mouse embryo fibroblast) or Vero E6 (African green monkey kidney) cells, by adsorption inoculation. After 1 h of adsorption, excess inoculum was discarded, the wells were washed twice with phosphate buffered saline and replaced by 1 ml of serum free MEM supplemented by 0.1 μ g/ml of L-1-tosylamide-2-phenylethyl chloromethyl ketone-treated trypsin (Sigma). Cultures were incubated at 37° C. with 5%

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CO_2 and inspected daily by inverted microscopy for cytopathic effects (CPE). After two to three weeks of incubation, subculturing to fresh cell line was performed even if there were no CPE and culture lysates were collected for RT-PCR for FmoPV. Immunostaining and electron microscopy were performed on samples that were RT-PCR positive for FmoPV.

CRFK and Vero E6 cells that were positive for FmoPV by RT-PCR were fixed in chilled acetone at -20° C. for 10 min. The fixed cells were incubated with 1:200 dilution of guinea pig antiserum against the N protein of FmoPV, followed by 1:50 diluted FITC-rabbit anti-guinea pig IgG (Invitrogen). Cells were then examined under fluorescence microscope. Uninoculated cells were used as negative control.

At the 8th passage, CRFK cells inoculated with a urine sample (761U) positive for FmoPV showed CPE at day 14, in the form of cell rounding, followed by cell detachment from the monolayer and cell lysis. At the 16th passage, CPE were evident at day 10 with syncytia formation (FIG. 6). RT-PCR for FmoPV using the culture supernatants and cell lysates showed positive results in CRFK cells inoculated with urine sample 761U and VeroE6 cells inoculated with supernatant of CRFK cells positive for FmoPV. Specific apple green finely granular and diffuse cytoplasmic fluorescence was also observed using serum from guinea pig immunized with recombinant N protein of FmoPV or corresponding serum of the infected cat (FIG. 6). Electron microscopy showed an enveloped virus with the typical "herring bone" appearance of the helical N in *paramyxoviruses* (FIG. 6). Virions are highly variable in size, ranging approximately from 130 to 380 nm in diameter. No CPE and no viruses were detected by RT-PCR in 3T3, B95 and CEF cells inoculated with the samples.

6.9 Example 9

Immunofluorescence Antibody Test

CRFK cells infected with FmoPV were fixed in chilled acetone at -20° C. for 10 min. The fixed cells were incubated with 4-fold dilutions of plasma from 1:10 to 1:10240 from the 27 cats with necropsies, followed by 1:20 diluted FITC-goat anti-cat IgG (Sigma). Cells were then examined under fluorescence microscope. Uninfected cells were used as negative control. Out of the 27 cats, immunofluorescent antibody was detected from 7 cats with titer from 1:40 to 1:640 (see Table 4, supra).

6.10 Example 10

Neutralizing Antibody Detection

100 TCID50 FmoPV were incubated with 2-fold dilutions of plasma from 1:10 to 1:2560 from the 27 cats with necropsies at 37° C. for 1 h. The mixtures were inoculated to 96-well plates of confluent CRFK cells. After 1 h of adsorption, the inoculum were removed and the plates were washed once with phosphate buffered saline and replaced by serum free MEM supplemented by 0.1 μ g/ml of L-1-tosylamide-2-phenylethyl chloromethyl ketone-treated trypsin (Sigma). The plates were incubated at 37° C. with 5% CO_2 for 7 days. The supernatants were removed and the cell monolayers were washed once with phosphate buffered saline and fixed in chilled methanol at -20° C. for 10 min. The fixed cells were incubated with 1:200 dilution of guinea pig antiserum against the N protein of FmoPV, followed by 1:50 diluted FITC-rabbit anti-guinea pig IgG (Invitrogen). Cells were then examined under fluorescence microscope. Cells infected with

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neutralized FMoPV showed no fluorescence. FMoPV infected cells were used as negative control. Out of the 27 cats, neutralization antibody was detected from 6 cats with titer from 1:20 to 1:40 (see Table 5, supra), of which all were positive for immunofluorescent antibody (see Table 4, supra).

6.11 Example 11

Histopathological Examination and Immunohistochemical Staining of FMoPV N Protein in Tissues and Cauxin Protein in Kidneys

To determine if FMoPV is associated with renal pathologies, such as TIN, histopathology and immunohistochemistry were performed on necropsy kidney tissues of two stray cats with positive FMoPV RT-PCR in their urine samples as described below, showing histopathological features compatible with TIN as well as detection of N protein of FMoPV in the renal tubules by immunohistochemistry.

Fixed necropsy organs of the two stray cats were embedded in paraffin. Tissue sections of 5 µm were stained with hematoxylin and eosin (H&E). Histopathological changes were observed using Nikon 80i microscope and imaging system. Expression of FMoPV N protein was examined by immunohistochemical staining. Tissue sections were deparaffinized and rehydrated, followed by blocking endogenous peroxidase with 3% H₂O₂ for 20 min, and then with 10% normal rabbit serum/PBS at room temperature for 1 h to minimize non-specific staining. The sections were incubated at 4° C. overnight with 1:250 dilution of guinea pig anti-N protein antiserum, followed by incubation of 30 min at room temperature with 1:500 dilution of biotin-conjugated rabbit anti-guinea pig IgG, H & L chain (Abeam) (30). Streptavidin/peroxidase complex reagent (Vector Laboratories) was then added and incubated at room temperature for 30 min. Color development was performed using 3,3'-diaminobenzidine and images captured with Nikon 80i imaging system and Spot-advance computer software. Double staining of lymph node was performed using mouse anti-human myeloid/histocyte antigen antiserum MAC387 (DakoCyomation) and labeled with Texas-red conjugated goat anti-mouse IgG (Jackson ImmunoResearch) (31). Cauxin protein expression was detected according to a published protocol (32).

Histological examination of various organs of two stray cats with FMoPV detected in urine revealed interstitial inflammatory infiltrate and renal tubular degeneration or necrosis in their kidneys (FIG. 10). In addition, there was also marked decrease in cauxin expression in the degenerated tubular epithelial cells, compatible with tubulointerstitial nephritis in cats with histological evidence of TIN (FIG. 11A), compared to cats without histological evidence of TIN where cauxin-positive proximal straight renal tubules were observed between the inner cortex and outer medulla (FIG. 11B). Immunohistochemical staining of their organs using guinea pig serum positive for anti-FMoPV N protein antibody revealed positive renal tubular cells in kidney sections and positive mononuclear cells in lymph node sections (FIG. 10). Using mouse anti-human myeloid/histocyte antigen antiserum MAC387, the targets of FMoPV in lymph node sections were shown to be macrophages (FIG. 12).

6.12 Example 12

Case Control Study

Among 27 stray cats, TIN was observed in 7 of 12 cats with evidence of FMoPV infection, but only in 2 of 15 cats without

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evidence of FMoPV infection ($P<0.05$ by Fisher's exact test) (Table 4). These results support a positive association between FMoPV infection (RT-PCR and/or antibody positivity) and TIN in cats.

The invention is not to be limited in scope by the specific embodiments described herein. Indeed, various modifications of the invention in addition to those described will become apparent to those skilled in the art from the foregoing description and accompanying figures. Such modifications are intended to fall within the scope of the appended claims.

All references cited herein are incorporated herein by reference in their entirety and for all purposes to the same extent as if each individual publication or patent or patent application was specifically and individually indicated to be incorporated by reference in its entirety for all purposes.

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 Gln Thr Arg Phe Ser Ala Gly Ser Tyr Pro Leu Leu Trp Ser Tyr Ala
 325 330 335

 Met Gly Val Gly Val Glu Leu Glu Arg Ser Met Gly Leu Asn Phe
 340 345 350

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Thr Arg Ser Phe Phe Asp Pro Thr Tyr Phe Arg Leu Gly Gln Glu Met
 355 360 365
 Val Arg Arg Ser Ser Gly Met Val Asn Ser Ser Phe Ala Arg Glu Leu
 370 375 380
 Gly Leu Ser Glu His Glu Thr Gln Leu Val Ser Gln Ile Val Asn Ser
 385 390 395 400
 Gly Gly Glu Ser Gly Ile Pro Lys Phe Asp Gly Phe Arg Ala Asn Pro
 405 410 415
 Thr Thr Phe Leu Gly Thr Lys Asp Asn Ile Asp Asp Arg Gly Glu Asp
 420 425 430
 Gln Ser Asn Ser Ile Ser Gly Leu Pro Gly Pro Leu Leu Pro Ser Arg
 435 440 445
 Asp Leu Asp Leu Ser Gly Asp Ser Tyr Gly Ile Asn Ser Gly Val Lys
 450 455 460
 Asn Val Ser Asp Lys Leu Asn Glu Gly Val Gly Pro Asp His Asp Val
 465 470 475 480
 Ser Ser Ser Ala Met Glu Glu Leu Arg Arg Leu Val Glu Ser Thr Asn
 485 490 495
 Arg Ile Asp Thr Lys Gln Pro Glu Ala Ser Gly Val Thr Asn His Tyr
 500 505 510
 Asn Asp Thr Asp Leu Leu Lys
 515

<210> SEQ ID NO 8
 <211> LENGTH: 519
 <212> TYPE: PRT
 <213> ORGANISM: Feline morbillivirus

<400> SEQUENCE: 8

Met Ser Ser Leu Leu Lys Ser Leu Ala Ala Phe Lys Arg His Arg Glu
 1 5 10 15

Gln Pro Thr Thr Pro Ser Gly Ser Gly Gly Thr Ile Lys Gly Leu Lys
 20 25 30

Asn Thr Ile Ile Val Pro Val Pro Gly Asp Thr Val Ile Thr Thr Arg
 35 40 45

Ser Asn Leu Leu Phe Arg Leu Val Tyr Ile Ile Gly Asn Pro Asp Thr
 50 55 60

Pro Leu Ser Thr Ser Thr Gly Ala Ile Ile Ser Leu Leu Thr Leu Phe
 65 70 75 80

Val Glu Ser Pro Gly Gln Leu Ile Gln Arg Ile Ala Asp Asp Pro Asp
 85 90 95

Ala Val Phe Lys Leu Val Glu Val Ile Pro Glu Ala Gly Asn Pro Gly
 100 105 110

Glu Leu Thr Phe Ala Ser Arg Gly Ile Asn Leu Asp Lys Gln Ala Gln
 115 120 125

Gln Tyr Phe Lys Leu Ala Glu Arg Asn Asp Gln Gly Tyr Tyr Val Ser
 130 135 140

Leu Gly Phe Glu Asn Pro Pro Asn Asp Asp Ile Thr Ser Ser Pro
 145 150 155 160

Glu Ile Phe Asn Tyr Ile Leu Ala Ser Val Leu Ala Gln Val Trp Ile
 165 170 175

Leu Leu Ala Lys Ala Val Thr Ala Pro Asp Thr Ala Ala Glu Ala Glu
 180 185 190

Asn Arg Arg Trp Ile Lys Leu Met Gln Gln Arg Arg Val Asp Gly Glu
 195 200 205

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Leu Arg Leu Ser Lys Gly Trp Leu Asp Leu Val Arg Asn Lys Ile Ala
 210 215 220
 Ser Asp Ile Thr Ile Arg Arg Phe Met Val Ala Leu Val Leu Asp Ile
 225 230 235 240
 Lys Arg Ser Pro Gly Thr Arg Pro Arg Ile Ala Glu Met Ile Cys Asp
 245 250 255
 Ile Asp Asn Tyr Ile Val Glu Ala Gly Leu Ala Ser Phe Leu Leu Thr
 260 265 270
 Ile Lys Phe Gly Ile Glu Thr Arg Tyr Pro Ala Leu Ala Leu His Glu
 275 280 285
 Phe Ser Gly Glu Leu Ala Thr Ile Glu Gly Leu Met Lys Leu Tyr Gln
 290 295 300
 Ser Met Gly Glu Met Ala Pro Tyr Met Val Ile Leu Glu Asn Ser Ile
 305 310 315 320
 Gln Thr Arg Phe Ser Ala Gly Ser Tyr Pro Leu Leu Trp Ser Tyr Ala
 325 330 335
 Met Gly Val Gly Val Glu Leu Glu Arg Ser Met Gly Gly Leu Asn Phe
 340 345 350
 Thr Arg Ser Phe Phe Asp Pro Thr Tyr Phe Arg Leu Gly Gln Glu Met
 355 360 365
 Val Arg Arg Ser Ser Gly Met Val Asn Ser Ser Phe Ala Arg Glu Leu
 370 375 380
 Gly Leu Ser Glu His Glu Thr Gln Leu Val Ser Gln Ile Val Asn Ser
 385 390 395 400
 Gly Gly Glu Ser Gly Ile Pro Lys Phe Asp Gly Phe Arg Ala Asn Pro
 405 410 415
 Thr Thr Phe Leu Gly Thr Lys Asp Asn Ile Asn Asp Lys Gly Glu Asp
 420 425 430
 Gln Ser Ser Ser Val Ser Gly Leu Pro Gly Pro Leu Leu Pro Ser Arg
 435 440 445
 Asp Leu Thr His Pro Gly Asp Ser Tyr Gly Ala Asp Asp Gly Val Lys
 450 455 460
 Asn Val Ser Asn Lys Leu Ser Glu Gly Ile Ser Pro Asp His Asp Val
 465 470 475 480
 Ser Ser Ser Ala Met Glu Glu Leu Arg Arg Leu Val Glu Ser Thr Asn
 485 490 495
 Arg Ile Asp Thr Lys Lys Pro Glu Ala Pro Gly Val Thr Asn His Tyr
 500 505 510
 Asn Asp Thr Asp Leu Leu Arg
 515

<210> SEQ_ID NO 9
 <211> LENGTH: 519
 <212> TYPE: PRT
 <213> ORGANISM: Feline morbillivirus

<400> SEQUENCE: 9

Met Ser Ser Leu Leu Arg Ser Leu Ala Ala Phe Lys Arg His Arg Glu
 1 5 10 15
 Gln Pro Thr Ala Pro Ser Gly Ser Gly Ala Ile Lys Gly Leu Lys
 20 25 30
 Asn Thr Ile Ile Val Pro Val Pro Gly Asp Thr Val Ile Thr Thr Arg
 35 40 45
 Ser Asn Leu Leu Phe Arg Leu Val Tyr Ile Ile Gly Asn Pro Asp Thr

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50	55	60
Pro Leu Ser Thr Ser Thr Gly Ala Ile Ile Ser	Leu Leu Thr Leu Phe	
65 65	70 75	80
Val Glu Ser Pro Gly Gln Leu Ile Gln Arg Ile Ala Asp	Asp Pro Asp	
85 85	90 95	
Ala Val Phe Lys Leu Val Glu Val Ile Pro Glu Ala Gly	Asn Pro Gly	
100 105	110	
Glu Leu Thr Phe Ala Ser Arg Gly Ile Asn Leu Asp	Lys Gln Ala Gln	
115 120	125	
Gln Tyr Phe Lys Leu Ala Glu Lys Asn Asp Gln Gly	Tyr Tyr Val Ser	
130 135	140	
Leu Gly Phe Glu Asn Pro Pro Asn Asp Asp Ile Thr Ser	Ser Pro	
145 150	155	160
Glu Ile Phe Asn Tyr Ile Leu Ala Ser Val Leu Ala Gln	Val Trp Ile	
165 170	175	
Leu Leu Ala Lys Ala Val Thr Ala Pro Asp Thr Ala Ala	Glu Ala Glu	
180 185	190	
Asn Arg Arg Trp Ile Lys Leu Met Gln Gln Arg Arg Val	Asp Gly Glu	
195 200	205	
Leu Arg Leu Ser Lys Gly Trp Leu Asp Leu Val Arg Asn	Lys Ile Ala	
210 215	220	
Ser Asp Ile Thr Ile Arg Arg Phe Met Val Ala Leu Val	Leu Asp Ile	
225 230	235	240
Lys Arg Ser Pro Gly Thr Arg Pro Arg Ile Ala Glu Met	Ile Cys Asp	
245 250	255	
Ile Asp Asn Tyr Ile Val Glu Ala Gly Leu Ala Ser Phe	Leu Leu Thr	
260 265	270	
Ile Lys Phe Gly Ile Glu Thr Arg Tyr Pro Ala Leu Ala	Leu His Glu	
275 280	285	
Phe Ser Gly Glu Leu Ala Thr Ile Glu Gly Leu Met Lys	Leu Tyr Gln	
290 295	300	
Ser Met Gly Glu Met Ala Pro Tyr Met Val Ile Leu Glu	Asn Ser Ile	
305 310	315	320
Gln Thr Arg Phe Ser Ala Gly Ser Tyr Pro Leu Leu Trp	Ser Tyr Ala	
325 330	335	
Met Gly Val Gly Val Glu Leu Glu Arg Ser Met Gly	Gly Leu Asn Phe	
340 345	350	
Thr Arg Ser Phe Phe Asp Pro Thr Tyr Phe Arg Leu	Gly Gln Glu Met	
355 360	365	
Val Arg Arg Ser Ser Gly Met Val Asn Ser Ser Phe	Ala Arg Glu Leu	
370 375	380	
Gly Leu Ser Asp His Glu Thr Gln Leu Val Ser Gln	Ile Val Asn Ser	
385 390	395	400
Gly Gly Glu Ser Gly Ile Pro Lys Phe Asp Gly	Phe Arg Ala Asn Pro	
405 410	415	
Thr Thr Phe Leu Gly Thr Lys Asp Asn Ile Asn Asp	Arg Gly Glu Asp	
420 425	430	
Gln Ser Asn Ser Ile Ser Gly Leu Pro Gly Pro Leu	Leu Pro Ser Arg	
435 440	445	
Asp Leu Asn Leu Ser Gly Asp Ser Tyr Gly Ile Asn Ser	Gly Val Lys	
450 455	460	
Asn Val Ser Asp Lys Leu Asn Glu Gly Val Gly Pro	Asp His Asp Val	
465 470	475	480

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Ser Ser Ser Ala Met Glu Glu Leu Arg Arg Leu Val Glu Ser Thr Asn
 485 490 495

Arg Ile Asp Thr Lys Gln Pro Glu Ala Ser Gly Val Thr Asn His Tyr
 500 505 510

Asn Asp Thr Asp Leu Leu Lys
 515

<210> SEQ ID NO 10
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
 6xHis tag

<400> SEQUENCE: 10

His His His His His His
 1 5

<210> SEQ ID NO 11
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
 primer

<400> SEQUENCE: 11

cagagactta atgaaaattta tgg 23

<210> SEQ ID NO 12
<211> LENGTH: 17
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
 primer

<400> SEQUENCE: 12

ccacccatcg ggtactt 17

<210> SEQ ID NO 13
<211> LENGTH: 4
<212> TYPE: PRT
<213> ORGANISM: Feline morbillivirus

<400> SEQUENCE: 13

Met Ser Ser Leu
 1

<210> SEQ ID NO 14
<211> LENGTH: 10
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
 oligonucleotide

<400> SEQUENCE: 14

ttaaaagggg 10

<210> SEQ ID NO 15
<211> LENGTH: 11
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

<400> SEQUENCE: 15

ttaaaaagggg g

11

<210> SEQ ID NO 16
<211> LENGTH: 10
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
oligonucleotide

<400> SEQUENCE: 16

ttaaaaagggg

10

<210> SEQ ID NO 17
<211> LENGTH: 22
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
primer

<400> SEQUENCE: 17

ttcatctctt agttcccagg aa

22

<210> SEQ ID NO 18
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
primer

<400> SEQUENCE: 18

ttcagactc accctcgata tct

23

<210> SEQ ID NO 19
<211> LENGTH: 23
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
primer

<400> SEQUENCE: 19

acgcggatcc gatgtctagt cta

23

<210> SEQ ID NO 20
<211> LENGTH: 26
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
primer

<400> SEQUENCE: 20

cggatttcgg ttttagaagg tcagta

26

<210> SEQ ID NO 21
<211> LENGTH: 523
<212> TYPE: PRT
<213> ORGANISM: Canine distemper virus

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<400> SEQUENCE: 21

Met Ala Ser Leu Leu Lys Ser Leu Thr Leu Phe Lys Arg Thr Arg Asp
1 5 10 15

Gln Pro Pro Leu Ala Ser Gly Ser Gly Ala Ile Arg Gly Ile Lys
20 25 30

His Val Ile Ile Val Leu Ile Pro Gly Asp Ser Ser Ile Val Thr Arg
35 40 45

Ser Arg Leu Leu Asp Arg Leu Val Arg Leu Val Gly Asp Pro Lys Ile
50 55 60

Asn Gly Pro Lys Leu Thr Gly Ile Leu Ile Ser Ile Leu Ser Leu Phe
65 70 75 80

Val Glu Ser Pro Gly Gln Leu Ile Gln Arg Ile Ile Asp Asp Pro Asp
85 90 95

Val Ser Ile Lys Leu Val Glu Val Ile Pro Ser Ile Asn Ser Ala Cys
100 105 110

Gly Leu Thr Phe Ala Ser Arg Gly Ala Ser Leu Asp Ser Glu Ala Asp
115 120 125

Glu Phe Phe Lys Ile Val Asp Glu Gly Ser Lys Ala Gln Gly Gln Leu
130 135 140

Gly Trp Leu Glu Asn Lys Asp Ile Val Asp Ile Glu Val Asp Asn Ala
145 150 155 160

Glu Gln Phe Asn Ile Leu Leu Ala Ser Ile Leu Ala Gln Ile Trp Ile
165 170 175

Leu Leu Ala Lys Ala Val Thr Ala Pro Asp Thr Ala Ala Asp Ser Glu
180 185 190

Met Arg Arg Trp Ile Lys Tyr Thr Gln Gln Arg Arg Val Val Gly Glu
195 200 205

Phe Arg Met Asn Lys Ile Trp Leu Asp Ile Val Arg Asn Arg Ile Ala
210 215 220

Glu Asp Leu Ser Leu Arg Arg Phe Met Val Ala Leu Ile Leu Asp Ile
225 230 235 240

Lys Arg Ser Pro Gly Asn Lys Pro Arg Ile Ala Glu Met Ile Cys Asp
245 250 255

Ile Asp Asn Tyr Ile Val Glu Ala Gly Leu Ala Ser Phe Ile Leu Thr
260 265 270

Ile Lys Phe Gly Ile Glu Thr Met Tyr Pro Ala Leu Gly Leu His Glu
275 280 285

Phe Ser Gly Glu Leu Thr Thr Ile Glu Ser Leu Met Met Leu Tyr Gln
290 295 300

Gln Met Gly Glu Thr Ala Pro Tyr Met Val Ile Leu Glu Asn Ser Val
305 310 315 320

Gln Asn Lys Phe Ser Ala Gly Ser Tyr Pro Leu Leu Trp Ser Tyr Ala
325 330 335

Met Gly Val Gly Val Glu Leu Glu Asn Ser Met Gly Gly Leu Asn Phe
340 345 350

Gly Arg Ser Tyr Phe Asp Pro Ala Tyr Phe Arg Leu Gly Gln Glu Met
355 360 365

Val Arg Arg Ser Ala Gly Lys Val Ser Ser Ala Leu Ala Ala Glu Leu
370 375 380

Gly Ile Thr Lys Glu Glu Ala Gln Leu Val Ser Glu Ile Ala Ser Lys
385 390 395 400

Thr Thr Glu Asp Arg Thr Ile Arg Ala Thr Gly Pro Lys Gln Ser Gln
405 410 415

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Ile Thr Phe Leu His Ser Glu Arg Ser Glu Val Ala Asn Gln Gln Pro
420 425 430

Pro Thr Ile Asn Lys Arg Ser Glu Asn Gln Gly Gly Asp Lys Tyr Pro
435 440 445

Ile His Phe Ser Asp Glu Arg Leu Pro Gly Tyr Thr Pro Asp Val Asn
450 455 460

Ser Ser Glu Trp Ser Glu Ser Arg Tyr Asp Thr Gln Ile Ile Gln Asp
465 470 475 480

Asp Gly Asn Asp Asp Asp Arg Lys Ser Met Glu Ala Ile Ala Lys Met
485 490 495

Arg Met Leu Thr Lys Met Leu Ser Gln Pro Gly Thr Ser Glu Asp Asn
500 505 510

Ser Pro Val Tyr Ser Asp Lys Glu Leu Leu Asn
515 520

<210> SEQ_ID NO 22

<211> LENGTH: 523

<212> TYPE: PRT

<213> ORGANISM: Dolphin morbillivirus

<400> SEQUENCE: 22

Met Ala Thr Leu Leu Arg Ser Leu Ala Leu Phe Lys Arg Asn Lys Asp
1 5 10 15

Arg Thr Pro Leu Ile Ala Gly Ser Gly Gly Ala Ile Arg Gly Ile Lys
20 25 30

His Val Ile Val Val Pro Val Pro Gly Asp Ser Ser Ile Val Thr Arg
35 40 45

Ser Arg Leu Leu Asp Arg Leu Val Arg Leu Ala Gly Asp Pro Tyr Ile
50 55 60

Ser Gly Pro Lys Leu Thr Gly Val Met Ile Ser Ile Leu Ser Leu Phe
65 70 75 80

Val Glu Ser Pro Ser Gln Leu Ile Gln Arg Ile Thr Asp Asp Pro Asp
85 90 95

Val Ser Ile Arg Leu Val Glu Val Ile Gln Ser Glu Lys Ser Leu Ser
100 105 110

Gly Leu Thr Phe Ala Ser Arg Gly Ala Asn Met Glu Asp Glu Ala Asp
115 120 125

Asp Tyr Phe Ser Ile Gln Ala Gly Glu Glu Gly Asp Thr Arg Gly Thr
130 135 140

His Trp Phe Glu Asn Lys Glu Ile Val Glu Ile Glu Val Gln Asp Pro
145 150 155 160

Glu Glu Phe Asn Ile Leu Leu Ala Ser Ile Leu Ala Gln Ile Trp Ile
165 170 175

Leu Leu Ala Lys Ala Val Thr Ala Pro Asp Thr Ala Ala Asp Ser Glu
180 185 190

Thr Arg Arg Trp Ile Lys Tyr Thr Gln Gln Arg Arg Val Val Gly Glu
195 200 205

Phe Arg Leu Asp Lys Gly Trp Leu Asp Ala Val Arg Asn Arg Ile Ala
210 215 220

Glu Asp Leu Ser Leu Arg Arg Phe Met Val Ala Leu Ile Leu Asp Ile
225 230 235 240

Lys Arg Thr Pro Gly Asn Lys Pro Arg Ile Ala Glu Met Ile Cys Asp
245 250 255

Ile Asp Thr Tyr Ile Val Glu Ala Gly Leu Ala Ser Phe Ile Leu Thr

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260	265	270
Ile Lys Phe Gly Ile Glu Thr Met Tyr Pro Ala Leu Gly Leu His Glu		
275	280	285
Phe Ser Gly Glu Leu Thr Thr Val Glu Ser Leu Met Asn Leu Tyr Gln		
290	295	300
Gln Met Gly Glu Thr Ala Pro Tyr Met Val Ile Leu Glu Asn Ser Ile		
305	310	315
Gln Asn Lys Phe Ser Ala Gly Ser Tyr Pro Leu Leu Trp Ser Tyr Ala		
325	330	335
Met Gly Val Gly Val Glu Leu Glu Asn Ser Met Gly Gly Leu Asn Phe		
340	345	350
Gly Arg Ser Tyr Phe Asp Pro Ala Tyr Phe Arg Leu Gly Gln Glu Met		
355	360	365
Val Arg Arg Ser Ala Gly Lys Val Ser Ser Ser Leu Ala Ala Glu Leu		
370	375	380
Gly Ile Thr Ala Glu Asp Ala Lys Leu Val Ser Glu Ile Ala Ala Gln		
385	390	395
Ala Asn Asp Asp Arg Ala Asn Arg Ala Ile Gly Pro Lys Gln Asn Gln		
405	410	415
Ile Ser Phe Leu His Pro Asp Arg Gly Asp Ala Ser Thr Pro Gly Asn		
420	425	430
Ile Leu Arg Ala Asn Glu Gly Asp Gly Ser Thr Arg Met Lys Arg Gly		
435	440	445
Gly Asn Ile Ala Thr Pro Lys Gly Thr Ser Ile Asp Gln Thr Ser Thr		
450	455	460
Thr Leu Ser Lys Asp Thr Leu Asp Ile Asp Glu Gln Ser Asp Asn Thr		
465	470	475
Asp Asp Pro Ile Ser Ile Gln Lys Ser Ala Glu Ala Leu Ala Lys Met		
485	490	495
Arg Ala Met Ala Lys Leu Leu Glu Asn Gln Gly Pro Arg Asp Val Thr		
500	505	510
Ala His Val Tyr Asn Asp Lys Asp Leu Leu Gly		
515	520	

<210> SEQ ID NO 23

<211> LENGTH: 525

<212> TYPE: PRT

<213> ORGANISM: Measles virus

<400> SEQUENCE: 23

Met Ala Thr Leu Leu Arg Ser Leu Ala Leu Phe Lys Arg Asn Lys Asp		
1	5	10
Lys Pro Pro Ile Thr Ser Gly Ser Gly Gly Ala Ile Arg Gly Ile Lys		
20	25	30
His Ile Ile Ile Val Pro Ile Pro Gly Asp Ser Ser Ile Thr Thr Arg		
35	40	45
Ser Arg Leu Leu Asp Arg Leu Val Arg Leu Ile Gly Asn Pro Asp Val		
50	55	60
Ser Gly Pro Lys Leu Thr Gly Ala Leu Ile Gly Ile Leu Ser Leu Phe		
65	70	75
Val Glu Ser Pro Gly Gln Leu Ile Gln Arg Ile Thr Asp Asp Pro Asp		
85	90	95
Val Ser Ile Arg Leu Leu Glu Val Val Gln Ser Asp Gln Ser Gln Ser		
100	105	110

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Gly Leu Thr Phe Ala Ser Arg Gly Thr Asn Met Glu Asp Glu Ala Asp
115 120 125

Gln Tyr Phe Ser His Asp Asp Pro Ser Ser Ser Asp Gln Ser Arg Ser
130 135 140

Gly Trp Phe Glu Asn Lys Glu Ile Ser Asp Ile Glu Val Gln Asp Pro
145 150 155 160

Glu Gly Phe Asn Met Ile Leu Gly Thr Ile Leu Ala Gln Ile Trp Val
165 170 175

Leu Leu Ala Lys Ala Val Thr Ala Pro Asp Thr Ala Ala Asp Ser Glu
180 185 190

Leu Arg Arg Trp Ile Lys Tyr Thr Gln Gln Arg Arg Val Val Gly Glu
195 200 205

Phe Arg Leu Glu Arg Lys Trp Leu Asp Val Val Arg Asn Arg Ile Ala
210 215 220

Glu Asp Leu Ser Leu Arg Arg Phe Met Val Ala Leu Ile Leu Asp Ile
225 230 235 240

Lys Arg Thr Pro Gly Asn Lys Pro Arg Ile Ala Glu Met Ile Cys Asp
245 250 255

Ile Asp Thr Tyr Ile Val Glu Ala Gly Leu Ala Ser Phe Ile Leu Thr
260 265 270

Ile Lys Phe Gly Ile Glu Thr Met Tyr Pro Ala Leu Gly Leu His Glu
275 280 285

Phe Ala Gly Glu Leu Ser Thr Leu Glu Ser Leu Met Asn Leu Tyr Gln
290 295 300

Gln Met Gly Glu Thr Ala Pro Tyr Met Val Ile Leu Glu Asn Ser Ile
305 310 315 320

Gln Asn Lys Phe Ser Ala Gly Ser Tyr Pro Leu Leu Trp Ser Tyr Ala
325 330 335

Met Gly Val Gly Val Glu Leu Glu Asn Ser Met Gly Gly Leu Asn Phe
340 345 350

Gly Arg Ser Tyr Phe Asp Pro Ala Tyr Phe Arg Leu Gly Gln Glu Met
355 360 365

Val Arg Arg Ser Ala Gly Lys Val Ser Ser Thr Leu Ala Ser Glu Leu
370 375 380

Gly Ile Thr Ala Glu Asp Ala Arg Leu Val Ser Glu Ile Ala Met His
385 390 395 400

Thr Thr Glu Asp Arg Ile Ser Arg Ala Val Gly Pro Arg Gln Ala Gln
405 410 415

Val Ser Phe Leu His Gly Asp Gln Ser Glu Asn Glu Leu Pro Gly Leu
420 425 430

Gly Gly Lys Glu Asp Arg Arg Val Lys Gln Gly Arg Gly Glu Ala Arg
435 440 445

Glu Ser Tyr Arg Glu Thr Gly Ser Ser Arg Ala Ser Asp Ala Arg Ala
450 455 460

Ala His Pro Pro Thr Ser Met Pro Leu Asp Ile Asp Thr Ala Ser Glu
465 470 475 480

Ser Gly Gln Asp Pro Gln Asp Ser Arg Arg Ser Ala Asp Ala Leu Leu
485 490 495

Arg Leu Gln Ala Met Ala Gly Ile Leu Glu Glu Gln Gly Ser Asp Thr
500 505 510

Asp Thr Pro Arg Val Tyr Asn Asp Arg Asp Leu Leu Asp
515 520 525

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<210> SEQ_ID NO 24
<211> LENGTH: 525
<212> TYPE: PRT
<213> ORGANISM: Peste-des-petits ruminants virus

<400> SEQUENCE: 24

Met Ala Thr Leu Leu Lys Ser Leu Ala Leu Phe Lys Arg Asn Lys Asp
1           5           10           15

Lys Ala Pro Thr Ala Ser Gly Ser Gly Gly Ala Ile Arg Gly Ile Lys
20          25           30

Asn Val Ile Ile Val Pro Ile Pro Gly Asp Ser Ser Ile Ile Thr Arg
35          40           45

Ser Arg Leu Leu Asp Arg Leu Val Arg Leu Ala Gly Asp Pro Asp Ile
50          55           60

Asn Gly Ser Lys Leu Thr Gly Val Met Ile Ser Met Leu Ser Leu Phe
65          70           75           80

Val Glu Ser Pro Gly Gln Leu Ile Gln Arg Ile Thr Asp Asp Pro Asp
85          90           95

Val Ser Ile Arg Leu Val Glu Val Gln Ser Thr Arg Ser Gln Ser
100         105          110

Gly Leu Thr Phe Ala Ser Arg Gly Ala Asp Leu Asp Asn Glu Ala Asp
115         120          125

Met Tyr Phe Ser Thr Glu Gly Pro Ser Ser Gly Gly Lys Lys Arg Ile
130         135          140

Asn Trp Phe Glu Asn Arg Glu Ile Ile Asp Ile Glu Val Gln Asp Pro
145         150          155          160

Glu Glu Phe Asn Met Leu Leu Ala Ser Ile Leu Ala Gln Val Trp Ile
165         170          175

Leu Leu Ala Lys Ala Val Thr Ala Pro Asp Thr Ala Ala Asp Ser Glu
180         185          190

Leu Arg Arg Trp Val Lys Tyr Thr Gln Gln Arg Arg Val Ile Gly Glu
195         200          205

Phe Arg Leu Asp Lys Gly Trp Leu Asp Ala Val Arg Asn Arg Ile Ala
210         215          220

Glu Asp Leu Ser Leu Arg Arg Phe Met Val Ser Leu Ile Leu Asp Ile
225         230          235          240

Lys Arg Thr Pro Gly Asn Lys Pro Arg Ile Ala Glu Met Ile Cys Asp
245         250          255

Ile Asp Asn Tyr Ile Val Glu Ala Gly Leu Ala Ser Phe Ile Leu Thr
260         265          270

Ile Lys Phe Gly Ile Glu Thr Met Tyr Pro Ala Leu Gly Leu His Glu
275         280          285

Phe Ala Gly Glu Leu Ser Thr Ile Glu Ser Leu Met Asn Leu Tyr Gln
290         295          300

Gln Leu Gly Glu Val Ala Pro Tyr Met Val Ile Leu Glu Asn Ser Ile
305         310          315          320

Gln Asn Lys Phe Ser Ala Gly Ala Tyr Pro Leu Leu Trp Ser Tyr Ala
325         330          335

Met Gly Val Gly Val Gly Leu Glu Asn Ser Met Gly Gly Leu Asn Phe
340         345          350

Gly Arg Ser Tyr Phe Asp Pro Ala Tyr Phe Arg Leu Gly Gln Glu Met
355         360          365

Val Arg Arg Ser Ala Gly Lys Val Ser Ser Val Ile Ala Ala Glu Leu
370         375          380

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Gly Ile Thr Ala Glu Glu Ala Lys Leu Val Ser Glu Ile Ala Ser Gln
385 390 395 400
Ala Gly Asp Glu Arg Thr Ala Arg Gly Thr Gly Pro Arg Gln Ala Gln
405 410 415
Val Ser Phe Leu Gln His Lys Thr Gly Glu Gly Glu Ser Ser Ala Pro
420 425 430
Ala Thr Arg Glu Gly Val Lys Ala Ala Ile Pro Asn Gly Ser Glu Glu
435 440 445
Arg Asp Arg Lys Gln Thr Arg Ser Gly Arg Pro Arg Gly Glu Thr Pro
450 455 460
Ser Gln Leu Leu Leu Glu Ile Met Pro Glu Asp Glu Val Ser Arg Glu
465 470 475 480
Ser Gly Gln Asn Pro Arg Glu Ala Gln Arg Ser Ala Glu Ala Leu Phe
485 490 495
Arg Leu Gln Ala Met Ala Lys Ile Leu Glu Asp Gln Glu Glu Gly Glu
500 505 510
Asp Asn Ser Gln Val Tyr Asn Asp Lys Asp Leu Leu Gly
515 520 525

<210> SEQ ID NO 25

<211> LENGTH: 525

<212> TYPE: PRT

<213> ORGANISM: Rinderpest virus

<400> SEQUENCE: 25

Met Ala Ser Leu Leu Lys Ser Leu Ala Leu Phe Lys Arg Ala Lys Asp
1 5 10 15
Lys Pro Pro Leu Ala Ala Gly Ser Gly Gly Ala Ile Arg Gly Ile Lys
20 25 30
His Val Ile Val Val Pro Ile Pro Gly Asp Ser Ser Ile Thr Thr Arg
35 40 45
Ser Arg Leu Leu Asp Arg Leu Val Lys Met Val Gly Asp Pro Asp Ile
50 55 60
Ser Gly Pro Lys Leu Thr Gly Ala Leu Ile Ser Ile Leu Ser Leu Phe
65 70 75 80
Val Glu Ser Pro Gly Gln Leu Ile Gln Arg Ile Thr Asp Asp Pro Asp
85 90 95
Ile Ser Ile Lys Leu Val Glu Val Gln Ser Asp Lys Thr Gln Ser
100 105 110
Gly Leu Thr Phe Ala Ser Arg Gly Thr Ser Met Asp Asp Glu Ala Asp
115 120 125
Arg Tyr Phe Thr Tyr Glu Glu Pro Asn Asp Gly Glu Glu Arg Gln Ser
130 135 140
Tyr Trp Phe Glu Asn Arg Asp Ile Gln Asp Ile Glu Ile Gln Asp Pro
145 150 155 160
Glu Gly Phe Asn Met Ile Leu Ala Thr Ile Leu Ala Gln Ile Trp Ile
165 170 175
Leu Leu Ala Lys Ala Val Thr Ala Pro Asp Thr Ala Ala Asp Ser Glu
180 185 190
Leu Arg Arg Trp Val Lys Tyr Thr Gln Gln Arg Arg Val Ile Gly Glu
195 200 205
Phe Arg Leu Asp Lys Gly Trp Leu Asp Thr Val Arg Asn Arg Val Ala
210 215 220
Glu Asp Leu Ser Leu Arg Arg Phe Met Val Ala Leu Ile Leu Asp Ile
225 230 235 240

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Lys Arg Thr Pro Gly Asn Lys Pro Arg Ile Ala Glu Met Ile Cys Asp
245 250 255

Ile Asp Thr Tyr Ile Val Glu Ala Gly Leu Ala Ser Phe Ile Leu Thr
260 265 270

Ile Lys Phe Gly Ile Glu Thr Met Tyr Pro Ala Leu Gly Leu His Glu
275 280 285

Phe Ala Gly Glu Leu Ser Thr Ile Glu Ser Leu Met Asn Leu Tyr Gln
290 295 300

Gln Met Gly Glu Leu Ala Pro Tyr Met Val Ile Leu Glu Asn Ser Ile
305 310 315 320

Gln Asn Lys Phe Ser Ala Gly Ala Tyr Pro Leu Leu Trp Ser Tyr Ala
325 330 335

Met Gly Ile Gly Val Glu Leu Glu Asn Ser Met Gly Gly Leu Asn Phe
340 345 350

Gly Arg Ser Tyr Phe Asp Pro Ala Tyr Phe Arg Leu Gly Gln Glu Met
355 360 365

Val Arg Arg Ser Ala Gly Lys Val Ser Ser Asn Leu Ala Ser Glu Leu
370 375 380

Gly Ile Thr Glu Glu Ala Arg Leu Val Ser Glu Ile Ala Ala Tyr
385 390 395 400

Thr Ser Asp Asp Arg Asn Asn Arg Thr Ser Gly Pro Lys Gln Ala Gln
405 410 415

Val Ser Phe Leu Arg Thr Asp Gln Gly Ser Glu Ala Gln His Ser Ala
420 425 430

Ser Lys Lys Asp Glu Ala Arg Ala Pro Gln Val Lys Lys Glu Thr Arg
435 440 445

Thr Ser Ser Lys Ser Asp Lys His Lys Glu Gly Thr Asp Lys Glu Pro
450 455 460

Val Ser Ser Ser Ala Met Thr Leu Ile Asp Val Asp Thr Thr Leu Glu
465 470 475 480

Ala Asp Thr Asp Pro Leu Glu Ser Lys Ser Ala Glu Ala Leu Leu
485 490 495

Arg Leu Gln Ala Met Ala Gly Ile Leu Gly Asp Ser Thr Leu Gly Asn
500 505 510

Asp Ser Leu Arg Ala Tyr Asn Asp Lys Asp Leu Leu Asn
515 520 525

<210> SEQ ID NO 26

<211> LENGTH: 523

<212> TYPE: PRT

<213> ORGANISM: Phocine distemper virus

<400> SEQUENCE: 26

Met Ala Ser Leu Leu Lys Ser Leu Ser Leu Phe Lys Lys Thr Arg Glu
1 5 10 15

Gln Pro Pro Leu Ala Ser Gly Ser Gly Gly Ala Ile Arg Gly Ile Lys
20 25 30

His Val Ile Ile Val Leu Ile Pro Gly Asp Ser Ser Ile Val Thr Arg
35 40 45

Ser Arg Leu Leu Asp Arg Leu Val Arg Met Val Gly Asp Pro Glu Val
50 55 60

Ser Gly Pro Lys Leu Thr Gly Val Leu Ile Ser Ile Leu Ser Leu Phe
65 70 75 80

Val Glu Ser Pro Gly Gln Leu Ile Gln Arg Ile Ile Asp Asp Pro Asp

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-continued

85	90	95	
Ile Ser Ile Lys Leu Val Glu Val Ile Pro Ser Ile Asn Ser Thr Cys			
100	105	110	
Gly Leu Thr Phe Ala Ser Arg Gly Ala Ser Leu Asp Ala Glu Ala Asp			
115	120	125	
Glu Phe Phe Gly Thr Met Asp Glu Gly Ser Lys Asp His Asn Gln Met			
130	135	140	
Gly Trp Leu Glu Asn Lys Asp Ile Ile Asp Ile Glu Val Asn Asp Ala			
145	150	155	160
Glu Gln Phe Asn Ile Leu Leu Ala Ser Ile Leu Ala Gln Ile Trp Ile			
165	170	175	
Leu Leu Ala Lys Ala Val Thr Ala Pro Asp Thr Ala Ala Asp Ser Glu			
180	185	190	
Met Arg Arg Trp Ile Lys Tyr Thr Gln Gln Arg Arg Val Ile Gly Glu			
195	200	205	
Phe Arg Met Asn Lys Ile Trp Leu Asp Ile Val Arg Asn Arg Ile Ala			
210	215	220	
Glu Asp Leu Ser Leu Arg Arg Phe Met Val Ala Leu Ile Leu Asp Ile			
225	230	235	240
Lys Arg Ser Pro Gly Asn Lys Pro Arg Ile Ala Glu Met Ile Cys Asp			
245	250	255	
Ile Asp Asn Tyr Ile Val Glu Ala Gly Leu Ala Ser Phe Ile Leu Thr			
260	265	270	
Ile Lys Phe Gly Ile Glu Thr Met Tyr Pro Ala Leu Gly Leu His Glu			
275	280	285	
Phe Ser Gly Glu Leu Thr Thr Ile Glu Ser Leu Met Val Leu Tyr Gln			
290	295	300	
Gln Met Gly Glu Thr Ala Pro Tyr Met Val Ile Leu Glu Asn Ser Val			
305	310	315	320
Gln Asn Lys Phe Ser Ala Gly Ser Tyr Pro Leu Leu Trp Ser Tyr Ala			
325	330	335	
Met Gly Val Gly Val Glu Leu Glu Asn Ser Met Gly Gly Leu Asn Phe			
340	345	350	
Gly Arg Ser Tyr Phe Asp Pro Ala Tyr Phe Arg Leu Gly Gln Glu Met			
355	360	365	
Val Arg Arg Ser Ala Gly Lys Val Ser Ser Thr Phe Ala Ala Glu Phe			
370	375	380	
Gly Ile Thr Lys Glu Glu Ala Gln Leu Val Ser Glu Ile Val Ser Arg			
385	390	395	400
Thr Thr Glu Asp Arg Thr Thr Arg Ala Thr Gly Pro Lys Gln Ser Gln			
405	410	415	
Ile Thr Phe Leu His Ser Glu Arg Asn Glu Ala Pro Asn Gln Arg Leu			
420	425	430	
Pro Pro Ile Thr Met Lys Ser Glu Phe Gln Gly Gly Asp Lys Tyr Ser			
435	440	445	
Asn Gln Leu Ile Asp Asp Arg Leu Ser Gly Tyr Thr Ser Asp Val Gln			
450	455	460	
Ser Ser Glu Trp Asp Glu Ser Arg Gln Ile Thr Gln Leu Thr Gln Glu			
465	470	475	480
Gly Asp His Asp Asn Asp Gln Gln Ser Met Asp Gly Leu Ala Lys Met			
485	490	495	
Arg Gln Leu Thr Lys Ile Leu Asn Gln Ser Asp Thr Asn Gly Glu Val			
500	505	510	

-continued

Ser Pro Ala His Asn Asp Arg Asp Leu Leu Ser
515 520

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<210> SEQ ID NO 27
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (2)..(2)
<223> OTHER INFORMATION: Any amino acid
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (4)..(4)
<223> OTHER INFORMATION: Ile or Val
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (5)..(7)
<223> OTHER INFORMATION: Any amino acid
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (9)..(9)
<223> OTHER INFORMATION: Ala or Cys
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (10)..(10)
<223> OTHER INFORMATION: Any amino acid
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<400> SEQUENCE: 27

Gln Xaa Trp Xaa Xaa Xaa Lys Xaa Xaa Thr
1 5 10

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<210> SEQ ID NO 28
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic
peptide
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (2)..(5)
<223> OTHER INFORMATION: Any amino acid
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (8)..(9)
<223> OTHER INFORMATION: Any amino acid
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (10)..(10)
<223> OTHER INFORMATION: Any aromatic amino acid
<220> FEATURE:
<221> NAME/KEY: MOD_RES
<222> LOCATION: (12)..(12)
<223> OTHER INFORMATION: Any aromatic amino acid
```

<400> SEQUENCE: 28

Phe Xaa Xaa Xaa Xaa Tyr Pro Xaa Xaa Xaa Ser Xaa Ala Met Gly
1 5 10 15

What is claimed is:

1. A method of detecting kidney disease in a feline comprising the steps of: (i) obtaining a sample from the feline; (ii) amplifying a DNA molecule derived from the sample using a set of primers that binds to the DNA molecule, wherein the primers are at least 95% identical to the nucleotide sequence of SEQ ID NO: 11, 12, 19, or 20; and (iii) detecting the amplified DNA molecule, which is at least 20 base pair in length, and wherein the feline is infected with a *morbillivirus*

and has kidney disease if the DNA molecule is at least 95% identical to the nucleotide sequence of FmoPV 776U, FmoPV M252A, or FmoPV 761U, and encodes the amino acid sequence of SEQ ID NO: 7, 8 or 9, respectively.

2. The method of claim 1 wherein the sample is a cell, blood, serum, plasma, saliva, urine, stool or sputum.

3. The method of claim 1 wherein the kidney disease is tubulointerstitial nephritis ("TIN").

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4. The method of claim 1 wherein the set of primers comprises a primer having the sequence of SEQ ID NO:11 or SEQ ID NO:12.

5. The method of claim 1 wherein the set of primers comprises primers having the sequences of SEQ ID NO:11 and 5 SEQ ID NO:12.

6. The method of claim 1 wherein the set of primers comprises a primer having the sequence of SEQ ID NO:19 or SEQ ID NO:20.

7. The method of claim 1 wherein the set of primers comprises primers having the sequences of SEQ ID NO:19 and 10 SEQ ID NO:20.

8. The method of claim 1 wherein the amplified DNA molecule is less than 200 base pair in length.

9. A method of diagnosing kidney disease in a feline comprising the steps of: (i) obtaining a sample from the feline; (ii) amplifying a DNA molecule derived from the sample using a set of primers that binds to the DNA molecule, wherein the primers are at least 95% identical to the nucleotide sequence of SEQ ID NO: 11, 12, 19, or 20; and (iii) detecting the 15 amplified DNA molecule, which is at least 20 base pair in length, and wherein the feline is infected with a *morbillivirus* and has kidney disease if the DNA molecule is at least 95% identical to the nucleotide sequence of FmoPV 761U, FmoPV 776U or FmoPV M252A, and encodes the nucleotide 20 sequence of SEQ ID NO: 1, 2 or 3, respectively. 25

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